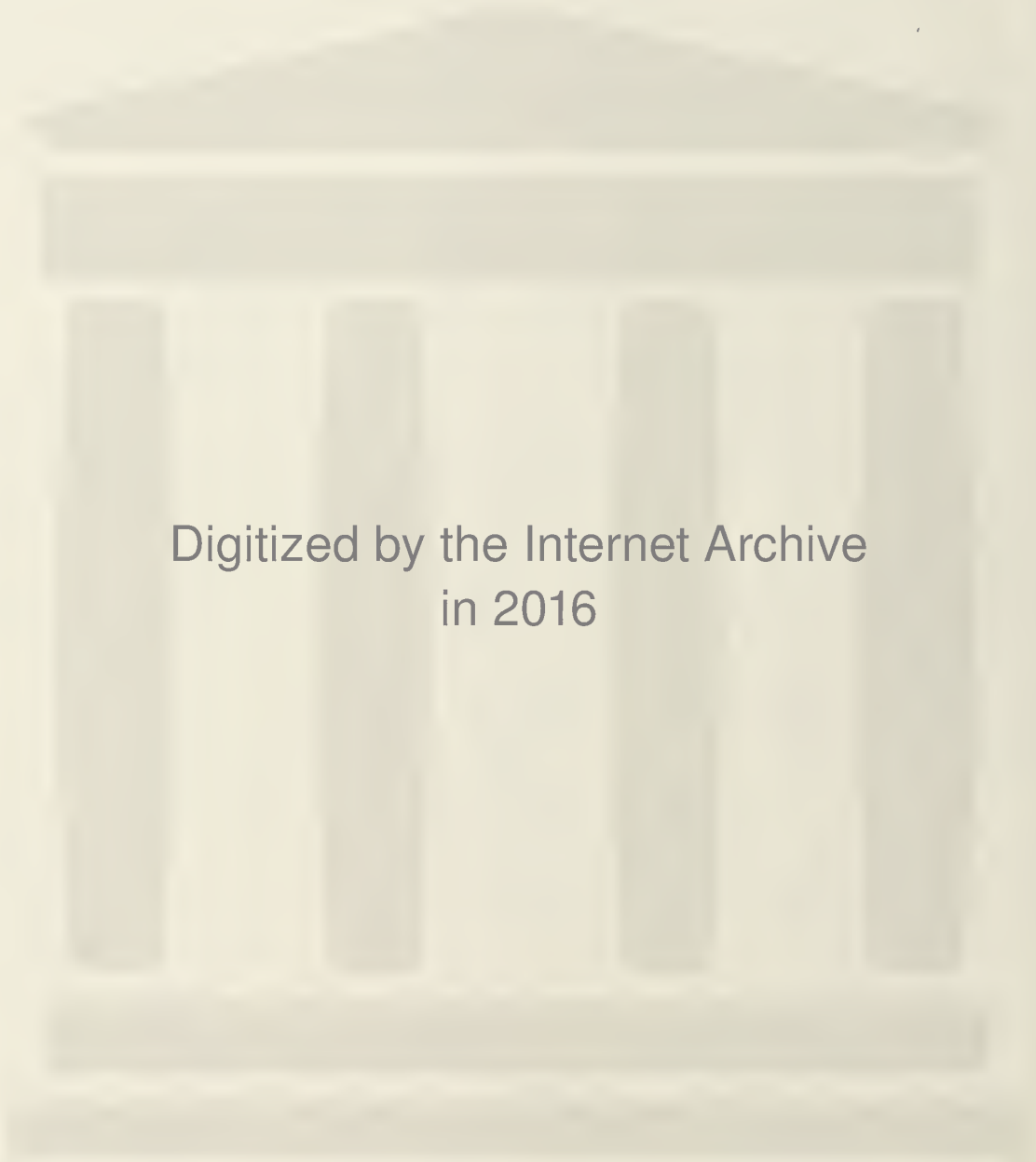
COUNTWAY LIBRARY
3 2044 115 035 362

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE
HARVARD MEDICAL LIBRARY-BOSTON MEDICAL LIBRARY


Digitized by the Internet Archive
in 2016

https://archive.org/details/rhodeislandmedic7019rhod

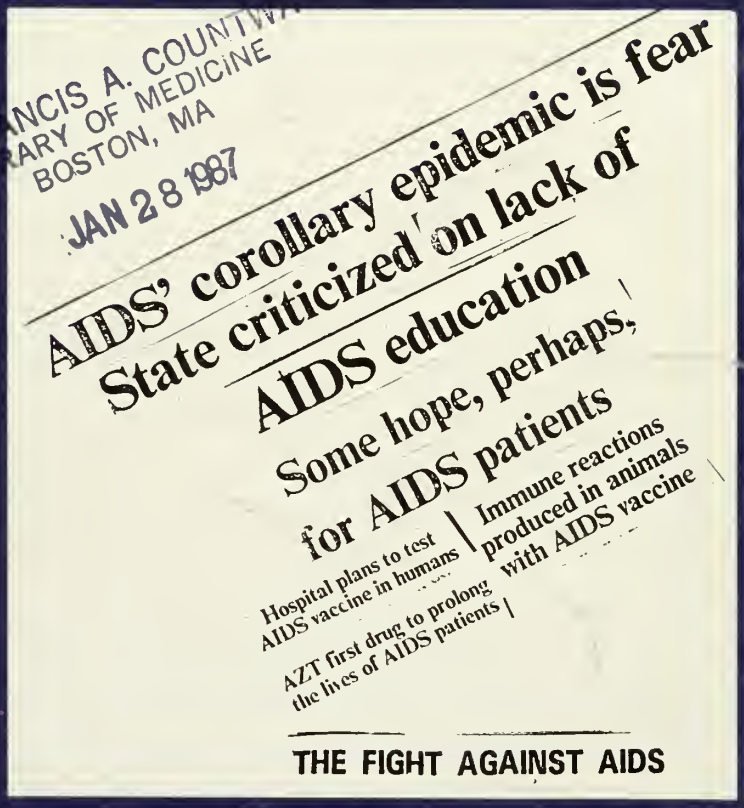
Rhode Island Medical Journal

January 1987
Volume 70, Number 1

DISPLAY SHELVES

Is Society Winning The Battle Against AIDS?

FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA
JAN 28 1987



CONTRIBUTIONS

11 AIDS and the Blood Supply

19 The Clinical Manifestations of the Acquired Immunodeficiency Syndrome

27 Therapeutic Approaches for AIDS and HIV Infection

35 The Epidemiology and Control of AIDS and HIV Infection in Rhode Island

9 EDITORIAL

43 SEMI-ANNUAL CALENDAR OF CONTINUING MEDICAL EDUCATION EVENTS

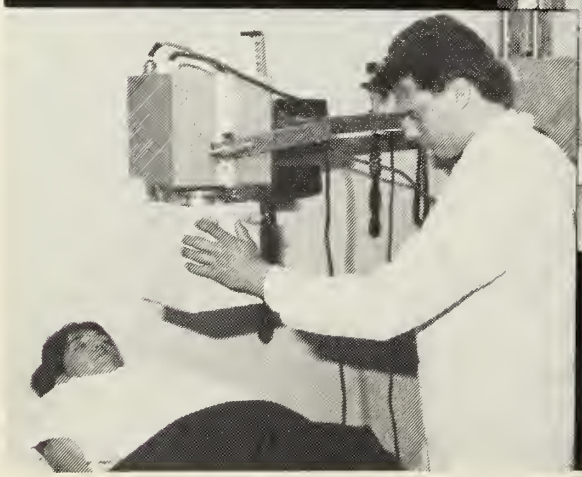
We've become the largest full service medical lab in Rhode Island...*because:*

- ✔ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✔ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✔ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✔ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Motrin® 800 mg TABLETS
ibuprofen

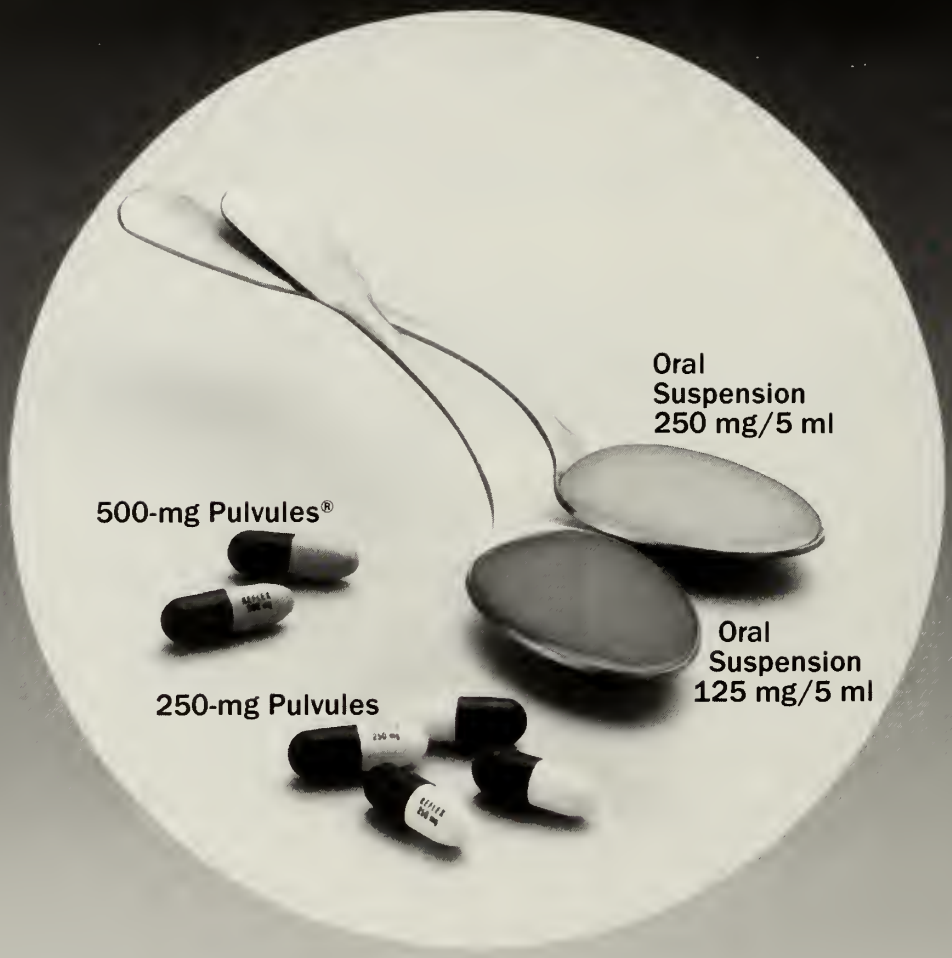
Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

Easy To Take



Keflex®
cephalexin

Additional information
available to the profession
on request.

DISTA

420113

Dista Products Company
Division of Eli Lilly and Company
Indianapolis, Indiana 46285
Mfd. by Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

Rhode Island Medical Journal

January 1987
Volume 70, Number 1

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

JAN 28 1987

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Jack A. Perkins
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Member of Publications Committee

***Guy A. Settipane, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

***Edward R. Feller, MD**

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***David T. Barrall, MD**
Resident

OFFICERS

Peter D. T. Clarisse, MD
President

Richard G. Bertini, MD
President-Elect

Milton W. Hamolsky, MD
Secretary

Kenneth E. Liffmann, MD
Treasurer

Herbert Rakatansky, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Vasant Gideon, MD
Kent County Medical Society

Thomas F. Cahill, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

John J. Coughlin, MD
Providence Medical Association

Vincent A. Montemarano, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph. 401 331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml (*1 teaspoonful*) contains: Guaifenesin, USP, 100 mg, Codeine Phosphate, USP, 10 mg (*warning: may be habit forming*), alcohol, 3.5 percent, in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

TABLE OF CONTENTS

5 **EDITORIAL**

The AIDS Epidemic

CONTRIBUTIONS

11 **AIDS and the Blood Supply**

Blood Banks Unwittingly Became a Vector in the Transmission of the Virus

Ronald A. Yankee, MD
Charles P. Mosher

19 **The Clinical Manifestations of the Acquired Immunodeficiency Syndrome: A Patient-Oriented Review**

Infectious Agents Are those that Take Advantage of the Immune Impairment

Alvan E. Fisher, MD

27 **Therapeutic Approaches for AIDS and HIV Infection**

An Effective Therapy or Preventive Vaccine Are Not Yet Available

Kenneth H. Mayer, MD
Steven M. Opal, MD

35 **The Epidemiology and Control of AIDS and HIV Infection in Rhode Island**

Alternative Testing Sites and Community Cooperative Efforts Are Features of Control Strategy

Richard A. Keenlyside, MD
L. Dondero
M. Corkery, RN
A. Johnson, RN

43 **SEMI-ANNUAL CALENDAR OF CONTINUING MEDICAL EDUCATION EVENTS**

COVER: *Headlines printed with permission from the Providence Journal Company, © 1986.*

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY.... ANYWHERE

PLUS insurance for....
tax audit
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

RP
REGENCY PLAZA

MEDICAL AND OFFICE SUITES

The Regency Plaza offers high quality medical and office suites:

- **within minutes of the major medical centers**
- **with direct access to routes 95 & 195**
- **with the convenience of downtown Providence**

In addition, we have

- **444 luxury apartments**
- **24 hour security**
- **convenient parking**

For more information call Debra Lipof at 861-6900.

Open daily 8-5
South on Rt. 95 — Atwells Exit.
North on Rt. 95 — Broadway Exit
(across from the Holiday Inn).

Managed by Chestnut Hill Realty Corp.

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

OFFICE SPACE AVAILABLE

due to retirement

E. Greenwich / Warwick, R.I.

Fully Equipped

Actively Functioning

Family Practice / Internal Medicine

Large building includes blood test lab in basement and upstairs apartment

401-884-4244
401-884-7357

GLEN, NEW HAMPSHIRE
Summit at Linderhof

CONDO For RENT

3 Bedroom Condo with spectacular mountain views. Sleeps 6 to 8. Fireplace, deck, cable TV, VCR, dishwasher, washer and dryer.

WITHIN 10 MINUTES of ALL MAJOR SKI AREAS.

(401) 949-2394

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℞

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

EDITORIAL

The AIDS Epidemic

The first published identification of the acquired immune deficiency syndrome (AIDS) is found in the June 5, 1981, issue of Morbidity and Mortality Weekly Report (MMWR) prepared by the US Centers for Disease Control (CDC). This issue briefly noted ". . . five young men, all active homosexuals, treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at three different hospitals in Los Angeles, California." The short paper also mentioned the coexistence of numerous opportunistic infections including cytomegalovirus and candidiasis. One of these five patients was an acknowledged parenteral drug abuser, and profoundly depressed numbers of thymus-dependent lymphocytes were demonstrated in three of the five patients. The authors considered the possibility of a cellular-immune dysfunction facilitating the infections and suggested the likelihood of an etiologic association between the new syndrome and some aspects of homosexual lifestyle or a new disease acquired through sexual contact.

One month later (July 3, 1981) MMWR described the presence of Kaposi's Sarcoma, an uncommonly reported malignancy, in 26 homosexual males, seven of whom also had pneumonia due to *Pneumocystis carinii*. These patients had also contracted a variety of concurrent infections including herpes simplex, cryptococcal meningitis and toxoplasmosis. Kaposi's Sarcoma, the authors stated, had previously been encountered only in elderly males, in patients receiving immunosuppressive therapy (such as renal transplant recipients) and in ". . . an endemic belt across equatorial Africa." The authors suggested that immunosuppression may activate some oncogenic virus resulting in Kaposi's Sarcoma.

During the next five years the Public Health Service's MMWR provided the medical profession with a stream of new epidemiologic and etiologic disclosures enlarging our knowledge of AIDS; and by June 11, 1982, 355 cases had been identified according to strict criteria established by the CDC. The major hypothesis offered was that ". . . infectious agents are being sexually transmitted among homosexually active males. Infectious agents not yet identified may cause the acquired cellular immunodeficiency." The July 9, 1982 MMWR issue reported concurrent opportunistic infections and Kaposi's Sarcoma in 34 Haitians residing in the United States, most also exhibiting severe T-cell dysfunction. The July 16, 1982 MMWR issue noted *Pneumocystis carinii* pneumonia among persons with hemophilia A, all of whom had received frequent injections of Factor VIII concentrate.

In September, 1982 MMWR summarized the CDC experience based upon 593 cases of AIDS. They observed that the number of diagnosed patients had roughly doubled each half-year since the syndrome was first identified. The list of opportunistic infections was now broadened to include cryptosporidiosis, atypical tuberculosis, aspergillosis, and nocardiosis. MMWR also periodically provided its readers with precautions for clinical and laboratory staffs working with AIDS patients or their biological fluids, observing that an infective agent is involved, but that it seems to require intimate direct mucosal surface contact or parenteral introduction for effective transmission.

The December 17, 1982 issue of MMWR described for the first time infants with combined immunodeficiency and opportunistic infections. Some of the the mothers of these infants were intravenous drug abusers, and the possibility of

a transplacental transmission of the AIDS virus was now entertained.

Immunodeficiency involving the female sexual partners of patients with AIDS was first noted in January, 1983. Clustering of AIDS cases in various US prison systems was observed at this time, and mention was made that many of these imprisoned individuals were, "regular users of intravenous drugs." By the end of 1982, the CDC had recorded 1,147 cases in 36 states and the District of Columbia. Rhode Island's first case was identified in this year.

By the end of 1985, the CDC registry of AIDS patients included 16,227 adults and 231 children fulfilling the stated definition of the syndrome. The number of AIDS cases reported each six-month interval continued to increase, although not exponentially as in the earlier years of the epidemic. Cases were still predominantly in homosexual/bisexual males, intravenous drug users, or both (collectively accounting for 90.4 per cent of all cases) while other high risk groups included hemophilia patients, transfusion recipients, heterosexual contacts of AIDS patients, and a small group born in Haiti. Among children with the syndrome, some were hemophiliacs, but most were infants of mothers with AIDS.

The US Public Health Service surveillance of AIDS continues. During 1986 various MMWR articles have addressed AIDS in military recruits, prison populations, and nations other than the United States.

During these six years of active recording, the CDC has made AIDS a notifiable disease, thus joining such public health threats as hepatitis, legionellosis, tuberculosis, and the venereal diseases. The cumulative number of reported cases of AIDS for the year 1986 as of September is 8,499, of which 375 originated in New England with 21 cases from Rhode Island. There had been 5,279 cases reported during the comparable 36 weeks of 1985. The tragic increase in cases continues.

In acknowledgement of the public health burden of AIDS, this issue of the *Journal* is devoted in its entirety to scientific articles on various aspects of the AIDS problem.

Stanley M. Aronson, M.D.

A Nursing Home
Striving to Provide
The Ultimate in Nursing Home
Service

100 Wampanoag Trail *East Providence*
401/438-4275

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

AIDS and the Blood Supply

Blood Banks Unwittingly Became a Vector in the Transmission of the Virus

Ronald A. Yankee, MD
Charles P. Mosher

Acquired immune deficiency syndrome (AIDS) was first recognized in the United States during the summer of 1981.[1-4] These initial cases were in young homosexually active males. In July 1982 papers published by the Center for Disease Control (CDC) implicated fractionated blood products as a possible cause in cases of immune suppression observed in hemophiliacs.[5] Numerical changes in various lymphocyte subpopulations in these patients had been observed, and the onset of clinical symptoms characteristic of AIDS suggested that factor VIII was in some way contributing to the development of this disease.[6,7] By December 1982 the first case of possible transfusion-associated acquired immune deficiency syndrome was published.[8,9] Since that time the health care system has focused considerable attention on the blood supply as a vector for the spread of AIDS beyond the original endemic populations which included sexually promiscuous homosexuals, present or past abusers of intravenous (IV) drugs and Haitian entrants to the United States.[10-13] Awareness of the potential for transmission of AIDS has served to sensitize the public not only to AIDS, but to other risks associated with blood transfusion. At the same time physicians now consider these risks more carefully in weighing the need for transfusion of blood or blood components.

Blood programs in the United States have generally been responsive to public concerns regarding the safety of blood. Prior to AIDS this concern was evident in the increasingly detailed medical evaluation required of all blood donors and the adoption of more stringent tests for hepatitis B required by the Standards of the American Association of Blood Banks (AABB) and the Food and Drug Administration (FDA).[14,15]

In early 1983, shortly after the CDC report suggesting that AIDS might be blood-borne, the blood banking organizations (AABB, American Red Cross [ARC] and the Council of Community Blood Centers [CCBC], in cooperation with the Public Health Service (PHS), developed recommendations to diminish the chance that high-risk individuals might donate blood. These recommendations were published March 4, 1983 and issued by the FDA on March 24.[16] These included educational programs to inform persons at increased risk not to donate and modification of the medical history to inquire about signs and symptoms of AIDS. In addition, the guidelines indicated that policies were to be developed for the disposition of suspected products. At the Rhode Island Blood Center informational brochures to be read prior to each blood donation were developed, standard operating procedures were revised, and the new recommendations were fully implemented by April 8, 1983.

Throughout 1983 further observations were made linking AIDS to transfusion. In a review of cases initially reported to the CDC it was recognized that the majority of transfusion recipients who developed AIDS were located in the four states where AIDS was most prevalent, ie, New York, California, New Jersey, and Florida.[10] Of the 18 post-transfusion AIDS cases analyzed, all had developed Pneumocystis carinii and all were without any known risk for AIDS. A suspect donor, either at high risk of AIDS or with abnormal T-cell (T4/T8, helper/suppressor) ratios was found in each of the most closely studied transfusion associated cases. AIDS developed in these recipients between 15 and 57 months (me-

Ronald A. Yankee, M.D. is the Director of the Rhode Island Blood Center, Providence, RI and Professor of Medicine, Brown University, Providence, RI.

Charles P. Mosher is the Administrative Director, Rhode Island Blood Center, Providence, RI.

dian 27.5) following transfusion. These observations suggested that AIDS was an infectious agent, transmissible through blood and most likely a virus. This view was substantiated when it was found that a retrovirus could be isolated and cultured from a large majority of patients with AIDS or pre-AIDS syndrome.[17-20] This virus, named human T-cell lymphotropic virus (HTLV-III) by the NIH group and lymphadenopathy associated virus (LAV) by the Pasteur Institute group, is recognized as the probable cause for AIDS. Its elucidation has provided a rational basis for research, for public health epidemiology, and for investigations into therapeutic intervention. It has recently been renamed human immunodeficiency virus (HIV).[21] Approximately one year following its discovery the Bureau of Biologics licensed screening tests for detection of antibody to HIV.[22] Although the screening tests were intended initially to be used by blood collection programs for screening blood donors, these test systems have been applied broadly as diagnostic indicators in cases where infection with AIDS virus is suspected.[23,24]

Method of HIV Antibody Testing

The Rhode Island Blood Center formally began testing for HIV antibody on March 21, 1985, and inventories were back tested to March 11, 1985. The test system employed is an enzyme linked immunoassay (ELISA or EIA) produced by Abbott Laboratories. In this system, plastic beads coated with viral antigen are reacted with donor serum or plasma. Reactivity is indicated by eliciting the presence of an immunoglobulin (the HIV antibody) attached to the antigen on the bead using an anti-immunoglobulin linked with horseradish peroxidase. A colorimetric reaction occurs when the enzyme is incubated with the appropriate substrate (phenylenediamine). The test is sensitive to technical variation, and all initially reactive samples must be repeated. Sera that are reactive on either of two repeat testings are considered "repeatedly reactive" and are tested further using the western blot immunoassay system. In this method the various proteins of HIV are separated electrophorectically by molecular weight and then bonded to nitrocellulose. Test sera or plasma that react with the protein bands specific for HIV are considered to contain HIV antibody.[25,26]

False-positive reactions are not uncommon in the very sensitive EIA assay. It is known for example that certain HLA antigens, DR4 in particular, which are derived from the cell lines used to culture the HIV, may be found as contaminants in the system.[27,28] Test sera containing anti-DR4 antibodies (eg, from a female previously sensitized during pregnancy) may interact with the DR4 on the bead and cause a false positive test result.[29-31] Such samples are found negative by the western blot test, but remain as repeatedly reactive in EIA and therefore unsuitable for transfusion.

The level of reactivity in the EIA concurs with western blot positivity, ie, the higher the ratio of the test result of the donor over the control value, the more likely that the sample will be found positive by western blot.[26] Repeatedly reactive individuals whose EIA tests ratios are between 7 and 13 are consistently found to be western blot positive. Other studies have shown similar findings, although more recent reports indicate that in certain individuals the western blot may be positive even at very low EIA test ratios.[32] Currently, blood that tests repeatedly positive in the EIA system is not used for transfusion regardless of whether or not positivity is confirmed by western blot.

There have been modifications in the EIA test system since the test was first licensed, and these have resulted in more consistent test results. The frequency of both initially and repeatedly-reactive test results has stabilized at lower levels (Figure 1) suggesting that a high proportion of early repeatedly reactive individuals were positive because of artifacts in these early test lots. Indeed

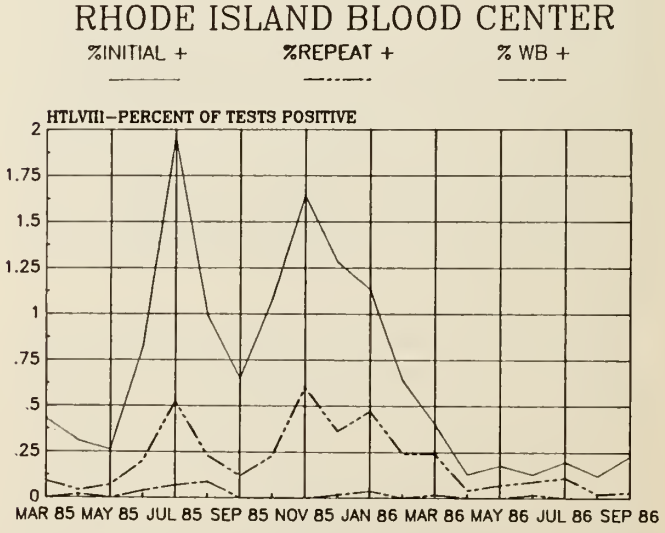


Fig 1. Results of HIV antibody testing of Rhode Island blood donors. Solid line shows initial test results and middle broken line indicates donors who are repeatedly positive. Western blot results are shown as lowermost broken line.

approximately 50 per cent of these individuals when tested for anti-HIV by EIA on subsequent donations are found to be negative. One of the dilemmas facing blood collection programs is whether or not to inform donors of these initial false positive reactions. Most collecting programs have considered the EIA repeatedly positive but western blot negative result a laboratory rather than clinical problem. Recently, however, it has been recommended by a National Institutes of Health (NIH) consensus group that these donors should be notified regardless of the psychological burden of being "stigmatized" by their HIV antibody status.[13] It is likely that most centers will heed the advice of this consensus panel despite strong reservations.

Table 1. Anti-HIV Results in Rhode Island Blood Donors 3/11/85-8/30/86

Total Donations Tested	79,789	
Initial EIA Reactive	546	0.68%
Repeatedly EIA Reactive	167	0.21%
Western Blot Positive	16	0.02%

HIV Antibody in Rhode Island Blood Donors

Between March 1985 and September 1986 HIV antibody tests have been performed on 79,789 blood donor samples in Rhode Island. Table 1 summarizes the test results. The prevalance of western blot-confirmed antibody in Rhode Island blood donors (.02 per cent) is similar to that of Boston (.03 per cent), Detroit (.03 per cent) and Philadelphia (.03 per cent). It is higher than Peoria (.011 per cent) and Tulsa (.003 per cent), but clearly lower than Washington DC (.11 per cent) and Los Angeles (.11 per cent). It should be emphasized that this represents the prevalence of HIV antibody in Rhode Island blood donors, not in the Rhode Island population. As previously mentioned, all blood donors undergo a pre-donation health screen, and individuals at high risk of AIDS are asked not to donate. It seems likely that the self-deferral program eliminates most of the high-risk individuals.[33-35]

Characteristics of Donors Positive for HIV

Sixteen individuals who donated blood were found to be western blot positive and were the subject of a notification procedure. This included a personal phone call by the Blood Center physician (or letter if contact could not be made by phone) for a scheduled visit to discuss the test results. The donors were counseled on the significance of the findings and need for instituting measures to prevent further spread of the virus according to the guidelines published by the PHS. The individuals were then referred to their own or to another physician for further examination and follow-up which included counseling and referral. Twelve of the 16 western blot-positive donors were interviewed and counseled. Two agreed to telephone contact only, and two are scheduled for interview at this time. One of the 16 donors was female with no known risk factors. Of the 13 males counseled, seven were homosexual, three had exchanged needles during intravenous drug abuse, and the remaining three are without known risk factors. No signs or symptoms of AIDS or AIDS-related complex were observed at the time of the initial interviews. One of the donors subsequently developed a rapidly progressive HIV encephalopathy and died approximately one year form discovery of seropositivity by the Blood Center. The finding of high risk factors in 71 per cent of these seropositive donors is similar to the experience of the American Red Cross in which 87 per cent of donors found positive for HIV antibody could be classified into one of the high-risk categories. In a study of transfusion-associated cases of AIDS, HIV was cultured from peripheral blood lymphocytes in over 95 per cent of the suspected high risk donors.[36] One can assume, therefore, that the presence of western blot confirmed antibody is presumptive evidence of current infection.

The "Look-Back" Program

It is now well-established that each of the components, eg, red cells, platelets, plasma, or cryoprecipitate, has the capacity to transmit HIV derived from blood donated by an HIV infected donor.[12] Heat treatment of Factor VIII concentrate appears to have successfully eliminated the risk of HIV transmission by this derivative in the treatment of Hemophilia A.[37] Although passive transfer of HIV antibody may occur with immunoglobulin preparations, transmission of HIV with Cohn-Oncley fractionated preparative does not appear to be a problem.[38-40] Among non-high-risk recipients, there does not appear to be a specific predisposition or susceptibility to the virus. HIV is readily transmitted, and evidence to date suggests that a high proportion of patients become infected after receiving blood or components from an HIV positive donor. Concern for this high rate of infectivity in recipients has prompted blood collecting programs to undertake investigation of all recipients of blood from prior donations of individuals who now test pos-

itive for HIV antibody. The purpose of the "look-back" program is to discover patients who may have received blood from donors at a time when the donor may have been infected with HIV. Patients who are found to be serologically positive can then be counseled on the steps to be taken to prevent further transmission of the virus to others. Guidelines for implementation of the "look-back" have been developed recently and distributed by the national blood banking organizations (AABB, ARC, and CCBC) following discussions with representatives from the American Hospital Association and public health agencies.

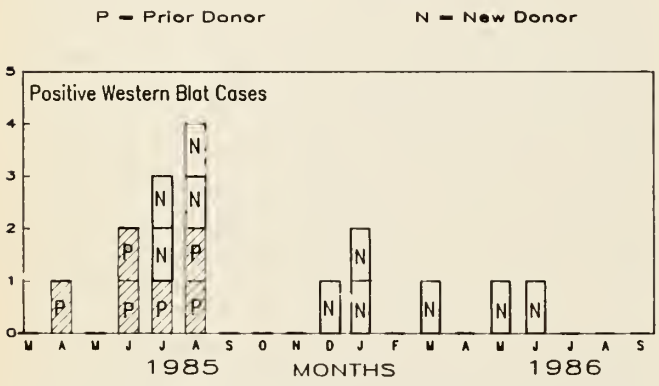


Fig 2. This shows the relative dates when individuals were found to be confirmed positive for antibody to HIV. Since August of 1985 *none* of the anti-HIV positive donors has a history of prior blood donations.

The Rhode Island Blood Center began implementation of its "look-back" in late spring of 1986. Six of the sixteen HIV antibody positive donors had donated prior to initiation of the HIV antibody test in March 1985. Figure 2 indicates the time relationship between identification of western blot positivity and prior donation history. This would appear to suggest that, from this time forward, most donors who will be found to be western blot positive will be new donors rather than individuals with a history of donations prior to March 1985.

From donations by these six individuals made prior to March 1985, there were 72 blood components that were transfused to patients. Sixty-six were transfused to patients in Rhode Island and six were delivered out of state to six facilities in five states. No information has been received regarding out-of-state transfusions.

Of the 66 recipients in Rhode Island, 37 died during the hospitalization at the time they received the blood or very shortly thereafter of their underlying disease. Due to the brief period between transfusion and death, no further follow-up of these patients or their families was indicated. The remaining 29 individuals and their families are the subjects of the "look-back" procedure.

The procedure is initiated by the Blood Center physician, who notifies the hospital blood bank director of the dates and unit numbers of the blood components involved. The blood bank director identifies the recipient of the unit and informs that patient's physician or the physician of record. It is the responsibility of the patient's physician to contact the patient and inform the person of the need for follow-up and serologic testing. Details of the "look-back" are shown in Table 2.

From information collected to date, it would appear that approximately 11 of the 29 living recipients in Rhode Island are at risk of seroconversion. It is not clear how many of these individuals will actually develop AIDS. It seems reasonable to postulate that the 12 individuals who have been tested or are suspected to be negative will remain so, having received blood presumably prior to the time when the donor became infected. Since, on average, AIDS becomes manifest at approximately three years from transfusion, it can be expected that most of the cases in Rhode Island will occur between the years

Table 2. Look Back Program

Implicated Donor	Recipients	Deceased	Tested or Suspected Positive	Tested or Suspected Negative	To Be Determined
A	23	13	6		4
B	17	8		7	2
C	12	6	3		3
D	8	5			3
E	8	5	2	1	
F	4	0		4	
	72	37	11	12	12

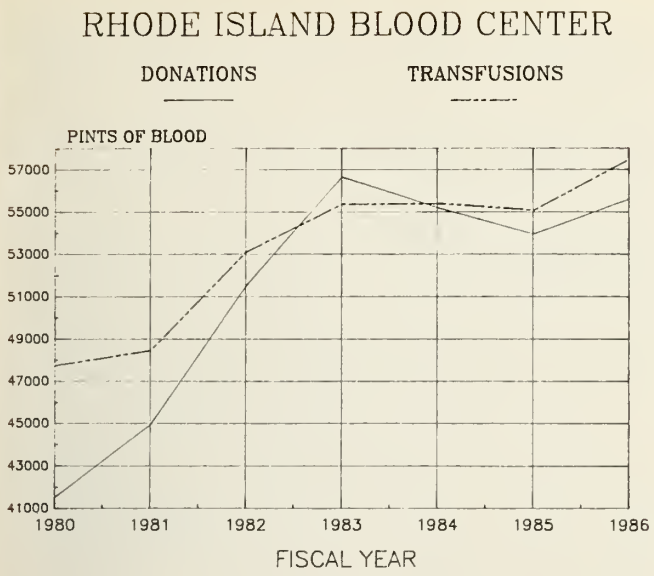


Fig 3. Relationship of annual blood donation (solid line) to blood transfusion (broken line) in Rhode Island from 1980 to 1986.

1987 and 1988. Thereafter, the full impact of screening donors and anti-HIV testing should result in a precipitous drop in the number of cases occurring.

Impact of AIDS on Blood Donation

Changing trends in blood donations and transfusions in Rhode Island from 1980 to 1986 are depicted in Figure 3. Intensification of blood donor recruitment and expansion of the Blood Center program appear to be responsible for the increase in blood donations beginning in 1980. In 1983 self-sufficiency was reached when donations exceeded transfusions by 3 per cent. During the following two years there was an unexplained leveling of transfusion activity, and at the same time donations began falling. By early 1984 it was clear that the blood supply had become unstable with less blood available than was needed for transfusion. Although these transfusion needs have been satisfied by importing blood from out of state, the deficit is widening due to a recent upswing in transfusions.

It is likely that the drop in blood donations is partly attributable to self-deferral of individuals who felt that they were in one or more of the defined high-risk categories. In addition, some individuals may have felt there was a possibility of becoming infected with the AIDS virus during the donation process. In mid-August of 1983 the Roper Organization conducted a survey of 2,000 individuals which measured public awareness and understanding of AIDS. This poll showed that 23 per cent of the population believed that AIDS could be contracted through the process of donating blood.[12] A small number of donors expressed concern that test results even if they were "false positive" might affect their futures either socially, medically, or legally. Whether or not these concerns have had a major impact on the blood supply is difficult to quantify, but measures to counter these concerns, in essence to reestablish public confidence that blood donation is safe, have been implemented.

Directed and Autologous Donations

In addition to the concerns expressed by volunteer donors, fear about the safety of blood has caused patients to seek alternatives to receiving blood from anonymous donors.

Autologous Donations

Autologous blood donation essentially eliminates the risks associated with blood-component incompatibility and disease transmission. Sensitization to red cells, white cells, and platelets is eliminated, and transfusion reactions are avoided. Procedures to carry out autologous blood donation are well established and generally are provided by most regional blood programs or transfusion services. This service has been available in Rhode Island since the opening of the Rhode Island Blood Center in 1979. A small increase in requests for autologous blood donation was first seen in early 1983 when it was first recognized that AIDS transmission could be associated with blood transfusion. At that time only 10 to 12 autologous blood donations per month were performed. This rate of autologous donation continued until March of 1985, when there was a sharp increase in interest concerning autologous donation associated with announcement of testing from anti-HIV antibody. The rate of autologous donation continues to increase and is currently at a minimum of 50 donations per month. Autologous donation represents approximately one per cent of the total blood donated annually in Rhode Island. Requests for autologous donations are initiated by physicians in the process of scheduling patients for elective surgery. In general, patients undergoing orthopedic, plastic, obstetric, or oral surgery are candidates.

Recently there has been a series of articles, especially in the lay press, advocating long-term storage of autologous blood. Promotion of these programs by entrepreneurs has stimated controversy. Most blood bankers and transfusion spe-

cialists discourage long-term cryopreservation for "just in case" circumstances based on the fact that it is unlikely that the autologous stored blood would be readily available for transfusion in the event that it was needed. The underlying assumption is that emergency blood transfusions cannot be effectively implemented using frozen blood. Currently, blood can be stored in the frozen state for three years, and processing costs approximately two-and-a-half times that of liquid blood.

Designated Donations

Fear of AIDs has prompted increasing numbers of requests for donations of blood to be directed to specific individuals. Such "designated donations" have been discouraged by policies enunciated by transfusion specialists in the major blood banking organizations (AABB, ARC, and CCBC). This policy was published in a joint statement issued by these organizations in June 1983. The policy generally recognizes that there is no clinical evidence that a designated donation offers improved safety over blood that is ordinarily donated by voluntary donors. There have been additional concerns expressed that increased numbers of designated donations may prove to be a serious cause of disruption of the blood supply, although evidence for this is lacking. Other concerns relate to donor eligibility requirements where individuals may feel pressured to provide less-than-truthful answers regarding past medical histories because of the pressure to donate from families and friends. Currently, the Rhode Island Blood Center does not provide this service.

Current Procedures to Safeguard the Blood Supply from AIDS

As previously mentioned beginning in 1983 the Rhode Island Blood Center put in place several mechanisms to protect the blood supply from AIDS. In brief these are as follows:

Educational program and self deferral. Each donor is now presented with an educational card describing signs, symptoms, and risk factors of AIDS. Anyone at risk is asked not to donate blood.

Donor medical history. The donor medical history has been modified to include questions regarding AIDS symptoms and risk factors. This includes both direct and indirect inquiries regarding: swollen glands, infection, self-injected drugs, unexplained weight loss, night sweats, fevers, diarrhea, skin tumors such as Kaposi's sarcoma, white spots or blemishes in the mouth, or exposure to a person with or at risk for AIDS. Additionally, the registration card is being revised to included in the donor consent a statement certifying that the donor is not at risk of transmitting disease.

Post donation instructions. Included in the post-donation instructions is a "call-back" mechanism for individuals who recognize that they are at risk but, because of peer pressure or fear of disclosure, must donate. A confidential telephone call allows these individuals to have their blood discarded immediately following donation.

Computer Deferral Registry. Prior to laboratory processing, an identifier code for each donor is entered into a computer for cross-checking against prior donation records. This assures that blood from any donor with a prior abnormal test result is not used for transfusion.

Anti-HIV Testing. A sample of blood from *each* donation is tested using the previously described procedure.

The Future

AIDS has added a new dimension to the administration of blood-collecting programs and blood-transfusion services. There is little doubt that there has been a major impact on heightening awareness to all risks associated with blood transfusion.

There is an urgent need for a test that would recognize HVI antigen, rather than antibody. This would eliminate the fear of transfusing blood from an HIV-infected donor who has not yet had time to develop detectable HIV antibody. The incidence of "false-negative" donors is estimated at between one case per 100,000-250,000 donations.[43] Only strong efforts to educate and screen out high-risk donors provides a measure of protection in this situation.

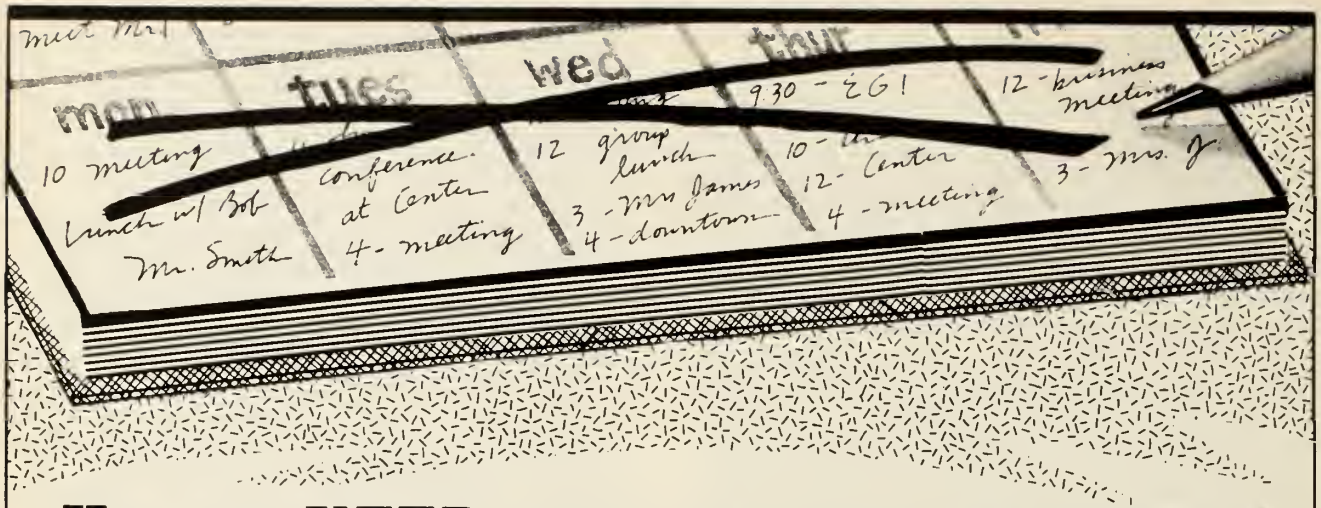
AIDS is a deadly disease which in the view of the public carries a social stigma associated with its origins. The media have sensed and played upon this hysteria. Blood banking, long dedicated to saving lives, finds itself the center of controversy, having become unwittingly one more vector for the transmission of HIV.

Acknowledgements

The authors acknowledge the laboratory contribution of Jane Petrucci and secretarial assistance of Gail Taylor.

References

1. Gottlieb MS, Schroff, R, Schanker HM, et al: Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Eng J Med 305:1425-31, 1981.
2. Friedman-Kien AE, Laubentein LJ, Rubenstein P, et al: Disseminated Kaposi's sarcoma in homosexual men. Ann Int Med 96:693-700, 1982.
3. Center for Disease Control. Pneumocystis pneumonia — Los Angeles. MMWR 30:250-2, 1981.
4. Center for Disease Control. Kaposi's sarcoma and pneumocystis pneumonia among homosexual men — New York City and California. MMWR 30:305-8, 1981.
5. Center for Disease Control. Pneumocystis carinii pneumonia among persons with hemophilia A. MMWR 31:365-7, 1982.
6. Lederman MM, Ratnoff OD, Scillian JJ, et al: Impaired cell-mediated immunity in patients with classic hemophilia. N Eng J Med 308:79-83, 1983.
7. Menitove JE, Aster RH, Casper JT, et al: T-lymphocyte subpopulation in patients with classic hemophilia treated with cryoprecipitate and lyophilized concentrates. N Eng J Med 308:83-6, 1983.
8. Center for Disease Control. Possible transfusion-associated acquired immune deficiency syndrome — California. MMWR 31:652-4, 1982.
9. Anmann AJ, Cowan MJ, Wara DW, et al: Acquired immunodeficiency in an infant: possible transmission by means of blood products. Lancet I:956-8, 1983.
10. Curran JW, Lawrence DN, Jaffe HW, et al: Acquired immunodeficiency syndrome (AIDS) associated with transfusion. N Eng J Med 310:69-75, 1984.
11. Jaffe HW, Sarngadharan MG, DeViso AL, et al: Infection with HTLVIII/LAV and transfusion-associated acquired immunodeficiency syndrome: serologic evidence of an association. JAMA 254:770-773, 1985.
12. Peterman TA, Jaffe HW, Feorino PM, et al: Transfusion-associated acquired immunodeficiency syndrome in the United States. JAMA 254:2913-17, 1985.
13. NIH Consensus Conference. The Impact of Routine HTLVIII Antibody Testing of Blood and Plasma Donors on Public Health. JAMA 256:1778-1783, 1986.
14. Schmidt PJ ed.: Standards for blood banks and transfusion services. 11th ed. Arlington, VA: American Association of Blood Banks, 1984.
15. Code of Federal regulations, H.H.S. FR36382:6604, 1979.
16. Center for Disease Control. Prevention of acquired immune deficiency syndrome (AIDS): Report of inter-agency recommendations. MMWR 32:101-103, 1983.
17. Barne-Sinoussi F, Chermann JC, Rey F, et al: Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 220:868-71, 1983.
18. Popovic M, Sarngadharan MG, Read E, et al: Detection, isolation and continuous production of cytopathic retroviruses (HTLVIII) from patients with AIDS and pre-AIDS. Science 224:500-3, 1984.
19. Gallo RC, Salahuddin SZ, Popovic M, et al: Frequent detection and isolation of cytopathic retroviruses (HTLVIII) from patients with AIDS and at risk for AIDS. Science 224:500-3, 1984.
20. Levy JA, Hoffman AD, Kramer SM, et al: Isolation of lymphocytopathic retroviruses from San Francisco patients with AIDS. Science 225:840-2, 1984.
21. International Committee on the Taxonomy of Viruses. Science 232:697, 1986.
22. Petricciani J: Licensed Tests for Antibody to Human T-Lymphotropic Virus Type III. Annal of Int Med 1985; 103:726-729.
23. Weiss SH, Goedert JJ, Sarngadharan MG, et al: Screening test for HTLVIII (AIDS agent) antibodies: specificity, sensitivity, and applications. JAMA 253:221-5, 1985.
24. Ward JW, Grindon AJ, Feorino PM, et al: Laboratory and epidemiologic evaluation of an enzyme immunoassay for antibodies to HTLVIII. JAMA 256:357-61, 1986.
25. Sarngadharan MG, Popovic M, Bruch L, et al: Antibodies reactive with human T-lymphotropic retrovirus (HTLVIII in the serum of patients with AIDS). Science 224:506-508, 1984.
26. Kleinman S, Anton-Guirgis H, Culver BD, et al: Anti-HTLVIII Elisa and Western Blot testing in a blood donor population: implications for donor notification. Vox Sang 51:143-147, 1986.
27. Kaplan HS, Kleinman SH: AIDS: blood donor studies and screening programs. Progr Clin Biol Res 182:297-308, 1985.
28. Osterholm MT, Bowman RJ, Chopeks MW, et al: Screening donated blood and plasma for HTLVIII antibody: facing more than one crisis? N Engl J Med 312:1185-1189, 1985.
29. Kuhnl P, Seidls S, Holzberger G: HLA DR4 antibodies cause positive HTLVIII antibody ELISA results. Lancet i:1222-1223, 1985.
30. Hunter JB, Menitove JE: HLA antibodies detected by ELISA HTLVIII antibody kits. Lancet ii:397, 1985.
31. Sayers MH, Beatty PG, Hansen JA: HLA antibodies as a cause of false positive reactions in screening enzyme immunoassays for antibodies to human T-lymphotropic virus Type III. Transfusion 26:113-115, 1986.
32. Kleinman S and Arens L: HTLVIII antibody testing in a higher risk AIDS area: absorbance value and test significance. Transfusion 25:480, 1985.
33. Pindyck J, Waldman A, Zang E, et al: Measures to decrease risk of acquired immunodeficiency syndrome transmission by blood transfusion. Evidence of volunteer donor cooperation. Transfusion 25:3-9, 1985.
34. Goedert JJ: Blood donation by persons at high risk of AIDS. N Eng J Med 312:1190, 1985.
35. Kalish RI, Cable RG and Roberts SC: Voluntary deferral of blood donations and HTLVIII antibody positivity. N Engl J Med 34:1115-1116, 1986.
36. Feorino PM, Jaffe HW, Palmer E, et al: Transfusion-associated acquired immunodeficiency syndrome: evidence for persistent infection in blood donors. N Engl J Med 312:1293-6, 1985.
37. Rouzioux C, Chamaret S, Montagnier L, et al: Absence of antibodies to AIDS virus in hemophiliacs treated with heat-treated factor VIII concentrate. Lancet i:271-72, 1985.
38. Report of the World Health Organization. Acquired immune deficiency syndrome: WHO meeting and consultation on the safety of blood and blood products. Wkly Epidem Rec 18:138-40, 1986.
39. Steele DR: HTLV-III antibodies in human immune gammaglobulin. JAMA 255:609, 1986.
40. White WB, Ryan RW, Staley DD, et al: Passive transfer of antibodies to human T-cell lymphotropic virus type III in patients receiving high-dose intravenous immunoglobulin. JAMA 255:2602, 1986.
41. Safety of therapeutic immune globulin preparations with respect to transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus infection. MMWR 35:231-233, 1986.
42. Council of Community Blood Centers. Roper Poll finds high awareness of AIDS: Misperception about blood donation and transfusion. CCBC Newsletter September 23, 1983.
43. Centers for Disease Control. Transfusion-Associated Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus Infection From a zeronegative Donor — Colorado. MMWR 35:389-391, 1986.



How to KEEP your Practice HEALTHY Even when YOU are NOT

IF you were disabled by accident or sickness, would your practice be disabled too?

The revenues of a professional office depend on the efforts of the doctor or doctors involved. If you or one of your associates is disabled and can not work, the office's income will suffer — income that's needed to pay overhead expenses.

You can protect your practice with Overhead Expense Insurance. While you're disabled, it pays expenses like office rent, employee salaries, utilities, taxes, and insurance premiums. You select the level of coverage that is best for your practice, and, as a member of a sponsoring organization, you can apply for coverage that may be more economical than an individual policy.

For more information, including costs, and what is and isn't covered, contact:

Endorsed by the
RHODE ISLAND MEDICAL SOCIETY

The Administrators
LB
personal service
since 1922
LESTER L. BURDICK, INC.
Loyalty Group Insurance
10 POST OFFICE SQUARE, BOSTON, MA 02109
(617) 426-0020

Underwritten by: **COMMERCIAL INSURANCE COMPANY** 15 Corporate Place South, Piscataway, NJ 08854. 201/981-4842

The Clinical Manifestations of the Acquired Immunodeficiency Syndrome: A Patient-Oriented Review

Infectious Agents Are those that Take Advantage of the Immune Impairment

Alvan E. Fisher, MD

The clinical manifestations of the acquired immodeficiency syndrome (AIDS) stem from the effect the causative virus has on the immune system. Human immunodeficiency virus (HIV; formerly human T-lymphotropic virus type III or lymphadenopathy-associated virus)[1] preferentially infects the T4 (helper) lymphocyte. This cell-specific infection directly causes the qualitative and quantitative T-cell defects that produce the characteristic clinical manifestations and complications of AIDS. I shall attempt to highlight some of the clinical problems encountered in patients with AIDS by a discussion of four patients recently seen at Rhode Island Hospital.

Patient 1. A 45-year-old white homosexual male who admitted to occasional intranasal and intravenous use of cocaine was initially evaluated at Rhode Island Hospital in June 1984. He was a resident of both New York City and Providence and presented with fatigue, malaise, weight loss, intermittent fevers, pancytopenia, and lymphadenopathy of several months duration. Kaposi's sarcoma (KS) was diagnosed in two small superficial lesions. The patient did well for four months when proctitis due to herpes simplex virus (HSV) occurred. In January 1985 Pneumocystis carinii pneumonia (PCP) was diagnosed by open lung biopsy. His treatment was complicated by adverse reactions to trimethoprim-sulfamethoxazole (TMP-sulfa) and pentamidine and by unexplained confusion and lethargy. In May 1985 he was hospitalized for bacterial pneumonia and alcohol abuse. His hospital stay was prolonged (112 days) and complicated by recurrent pneumonia, disseminated cytomegalovirus (CMV) infection with acute chorioretinitis, and progressive encephalopathy with seizures. He died in September, 15 months after the initial diagnosis of AIDS.

Patient 2. A 25-year-old white homosexual male who lived in New York City developed KS in October 1984. Two months later he developed PCP complicated by adverse reaction to TMP-sulfa. In June 1985 PCP recurred, but treatment with TMP-sulfa was uncomplicated. Oral candidiasis and persistent localized herpes zoster occurred. Three months later he moved to his parents' home in Rhode Island. Extensive KS required systemic chemotherapy and radiation therapy. In October 1985 sudden visual impairment due to acute chorioretinitis was noted consistent with that due to CMV infection. Antiviral therapy with the investigational parenteral drug DHPG was begun and continued at home via Hickman catheter. This treatment was complicated four months later by bacteremia due to coagulase-negative staphylococci. The patient had progressive extensive KS, weight loss, nausea, and vomiting. He died in March 1986, 17 months after the initial diagnosis of AIDS.

Patient 3. A 49-year-old white homosexual male residing in Providence presented with fever and weight loss in October 1984. Laboratory evaluation revealed leukopenia, lymphopenia, and serological evidence of HIV and Epstein-Barr virus (EBV) infection. Six months later splenomegaly was demonstrated by computed tomog-

Alvan E. Fisher, MD is Clinical Instructor at Brown University Program in Medicine, Providence, Rhode Island and Staff Physician, Department of Medicine, Rhode Island Hospital, Providence, RI

raphy (CT). Oral candidiasis, progressive weight loss, and fever were present. A serologic test for HIV was positive. The patient experienced episodes of unexplained disorientation and was admitted to Rhode Island Hospital for further evaluation in October 1985. Electroencephalogram (EEG) and cranial CT were consistent with diffuse encephalopathy. Cerebrospinal fluid (CSF) examination revealed a lymphocytic pleocytosis. He was unable to work due to increasing difficulty with cognitive functioning. Neuropsychiatric evaluation was planned, but while visiting his family in New York State in December he experienced severe mental status deterioration complicated by pneumonia and died six weeks later.

Patient 4. A 36-year-old bisexual white male resident of Providence developed PCP in June 1985. Diarrhea caused by Cryptosporidium proved persistent and refractory to both specific (spiramycin and furazolidone) and to nonspecific treatments. He volunteered for suramin therapy at the National Institutes of Health in Bethesda, Maryland, but his course of therapy was terminated due to severe toxicity. Genital, perianal, and cutaneous HSV infections were persistent and moderately controlled with parenteral acyclovir. The cryptosporidiosis caused severe malnutrition and weight loss requiring total parenteral nutrition in December 1985. Episodes of duodenitis, pancreatitis, and cholangitis were apparently due to Cryptosporidium. By April 1986 he developed symptoms of confusion, disorientation, and dementia. Fever, weight loss, and profuse diarrhea continued. Several attempts at home care had been successful, but the patient was readmitted to Rhode Island Hospital in May and expired less than 12 hours later.

These cases are illustrative of many points concerning the clinical manifestations of AIDS. AIDS is a syndrome characterized by a specific immunological defect of the T-lymphocytes. Extensive dysfunction of the entire immune system typically occurs, but the complications tend to be those due to the HIV infection itself or to the T-cell impairment.

Prodrome

Most patients have prodromal symptoms such as fever, weight loss, or malaise for weeks or months prior to the diagnosis of AIDS.[2] These prodromal symptoms are nonspecific and not diagnostic of AIDS as currently defined. The Centers for Disease Control (CDC) in Atlanta has recently developed a classification system for HIV infection based on the clinical manifestations and natural history of HIV infection.[3] As more information is accumulated about the natural history of HIV infection, this classification scheme should prove helpful in the assessment of patients, especially in early stages. For the present the diagnosis of AIDS still requires the documentation of a specific opportunistic infection or secondary malignant disease associated with T-cell dysfunction in the absence of any cause of T-cell dysfunction other than HIV infection.

During the prodromal period patients may be clinically stable for months or may rapidly progress to the clinical diagnosis of AIDS. Indeed, the clinical diagnosis of AIDS may never be established, and the patient may succumb to other complications (patient 3).

Secondary Malignant Tumors

Kaposi's sarcoma is a malignant lesion that most physicians in the United States had never seen prior to 1981.[4] It occurred mostly in older men of Mediterranean ancestry and was typically indolent and confined to the skin of the lower extremities. KS is now diagnosed mostly in young men with AIDS. It is the initial manifestation of AIDS in approximately 30 per cent of cases.[5] The clinical course of KS in AIDS is highly variable. As with patient 1 there may be but a few small lesions, or there may be extensive distribution with rapid progression (patient 3). Lesions are located on the trunk, upper and lower extremities, and head and neck and are frequently associated with soft-tissue infiltration. Lesions may commonly involve mucous membranes, the gastrointestinal tract, or lymph nodes. Involvement of all other internal organs except the brain has been reported. Successful treatment regimens have included radiation therapy for localized disease and chemotherapy for disseminated disease. Surgical resection (as with patient 1) may be curative though most patients have multiple lesions which precludes surgery. Some patients with AIDS and KS will have prolonged survival. Most develop opportunistic infections and will succumb to the consequences of progressive immunodeficiency.

Other malignant conditions associated with AIDS include Hodgkin's and non-Hodgkin's lymphomas, acute and chronic lymphocytic leukemia, and squamous cell carcinoma of the anus.[6] Though relatively few in number, these cases are marked by frequent opportunistic infections, marked immunosuppression, and poor prognosis.

Opportunistic Infections

Many physicians are frustrated by the seemingly overwhelming number of opportunistic infections that can occur: "AIDS patients can get anything." However, patients with AIDS cannot in fact get anything; they are susceptible to those organisms that take advantage of the underlying T-cell dysfunction.[7] Thus PCP not S pneumoniae causes most pulmonary infection.[8] M avium not S aureus causes most bacteremia,[9] and Cryptococcus neoformans not N meningitidis causes most meningitis.[10] The infectious complications of AIDS are exasperating since most of the infecting organisms are unfamiliar to many physicians (including infectious disease specialists) and treatment involves unfamiliar drugs and unusual adverse reactions.

Pulmonary Complications

Pneumocystis carinii is the most common cause of pulmonary infection and causes the most common serious opportunistic infection in persons with AIDS.[11] Prior to the AIDS epidemic PCP was a rare complication in immunocompromised patients. The diagnosis of PCP requires demonstration of the organism in clinical specimens from the respiratory tract. Bronchoalveolar lavage has become the most common and reliable technique[8] (patients 2 and 4), though some cases require transbronchial or open lung biopsy (patient 1) for diagnosis. Noninvasive methods for diagnosis of PCP include pulmonary function testing, gallium and technesium scanning, and serology.[12] These noninvasive methods are generally sensitive, but non-specific for the diagnosis of PCP. Treatment of PCP is usually successful using either pentamidine or TMP-sulfa, although adverse reactions are common with either therapy.[13] Dapsone with or without trimethoprim[14] or eflornithine,[15] an investigational agent, has been used as alternatives. Recurrence after therapy (patient 2) is frequent, and life-long prophylaxis with TMP-sulfa is usually administered if possible.

Other causes of pulmonary infection include CMV, M avium, and M tuberculosis as well as S pneumoniae, H influenzae, and S aureus. KS is another rare cause of pulmonary infiltration.

Gastrointestinal Complications

Gastrointestinal (GI) involvement in persons with AIDS can be persistent and progressive, and is a frequent cause of the wasting and weight loss associated with AIDS (patient 4). Both common and uncommon pathogens affect the GI tract. In patient 4 cryptosporidiosis was the major cause of the patient's decline and death. A recognized pathogen in horses and other animals, Cryptosporidium was previously rarely documented in humans and usually only in individuals with animal exposure. In these individuals the infection is usually self-limited. In persons with AIDS cryptosporidiosis is usually protracted and frequently produces overwhelming life-threatening diarrhea.[11] Involvement of the biliary tree, as in patient 4 is rare but has been reported.[16] Involvement of the lung has also been reported.[17] Treatment with either investigational (spiramycin, bovine transfer factor, eflornithine) or noninvestigational (furazolidone, tetracycline, metronidazole) agents is usually unsuccessful.[18] Nonspecific therapy with antimotility agents and fluids can be helpful. Other parasites such as Giardia lamblia, Entamoeba histolytica, or Isospora belli are common in persons with AIDS and in homosexual men without HIV infection. Generally these organisms do not cause more severe symptoms in the presence of HIV infection.

The GI tract serves as the portal of entry for two common bacterial infections in persons with AIDS, Salmonella species and Mycobacterium avium intracellulare. Both of these organisms produce significant disseminated infection without prominent GI manifestations. Other GI pathogens include CMV, HSV, Shigella species, and Campylobacter fetus.

CNS Complications

Involvement of the central nervous system (CNS) is unfortunately almost universal in persons with AIDS.[19] In the first few years of the AIDS epidemic Toxoplasma gondii was the most commonly reported cause of encephalitis.[20] Cryptococcus neoformans was the most common cause of meningitis.[10] Both infections produce significant CNS manifestations and require life-long therapy to prevent relapse. Since 1983 an increasing number of reports have described the progressive encephalopathy that accompanies AIDS. HIV has now been shown to be neurotropic and can infect both central and peripheral neurons.[21] It can produce subcortical dementia, which is the commonest CNS complication in AIDS.[22] A variety of peripheral neuropathic syndromes may result from infection of peripheral neurons. "AIDS-dementia" can present with symptoms mimicking depression (which is also quite common in AIDS) and can progress to a profound impairment of CNS function. This primarily affects cognitive processes, but also may

produce seizures and myoclonus (patients 1,3, and 4). The course in these patients is usually slowly progressive over months (patient 1). A more rapid decline within a few weeks is not uncommon (patients 3 and 4). Patient 3 demonstrates that CNS dysfunction can precede the development of opportunistic infection or secondary malignancy. Indeed, nearly one-quarter of patients with AIDS dementia seen at Memorial Sloan-Kettering Cancer Center in New York City presented or died with symptomatic neurological dysfunction prior to fulfilling the CDC criteria for the diagnosis of AIDS.[23]

The psychosocial and psychiatric sequelae of AIDS affect the patients and their friends and families, as well as health care workers. Several approaches to the management of psychosocial stress in health-care workers caring for persons with AIDS have been published.[22,24]

Other Complications

Mycobacterium avium-intracellulare (MAI) is the commonest cause of bacteremia in AIDS.[9,11] Disseminated infection has been found at autopsy in over one-half of persons with AIDS.[25] Cultures of blood and bone marrow aspirates are most likely to demonstrate this organism antemortem, though at autopsy isolation from all internal organs has been reported. Treatment of disseminated infection seems to require a multidrug regimen usually including the investigational agents ansamycin (rifabutin) and clofazimine as well as two or three standard antimycobacterial drugs. Response to therapy has been variable. Many, if not most, patients continue to have active infection with positive cultures, but some will have a clinical response.[25]

Bacteremia due to Salmonella species is common and usually persistent, requiring life-long therapy.[26] Other causes of bacteremia relate to invasive procedures: ie coagulase-negative staphylococci or S aureus associated with indwelling vascular catheters.[9]

Cytomegalovirus, herpes simplex, and varicella-zoster virus (VZV) are frequent pathogens in persons with AIDS.[27] CMV has been implicated as a causative agent of persistent fever, chorioretinitis, invasive pneumonitis, and colitis. Several investigational agents such as DHPG and foscarnet have shown activity against these syndromes. Unfortunately, prolonged therapy seems necessary, as relapses and recurrences are common if treatment if discontinued.

HSV infections are common, persistent, and frequently severe (patient 4). The most common site is the perianal region causing extensive superficial ulceration. Oral, esophageal, and cutaneous infection also occurs. VZV usually causes the typical lesions of herpes zoster, but these lesions may persist, recur, or disseminate (patient 2). Acyclovir is effective therapy for both HSV and VZV. Prolonged therapy (frequently parenteral) is usually required as in patient 4.

Fever is a common problem in persons with AIDS. Fever may be low-grade or high, intermittent or persistent with single, multiple, or no demonstrable cause. Any of the infections associated with AIDS may cause fever, but the more obscure cases may be caused by MAI, CMV, PCP (with normal chest x-ray), or possibly HIV itself. Empiric antimicrobial therapy is generally not indicated because of the high likelihood of toxicity associated with many of the therapeutic agents.

Summary

The clinical manifestations of AIDS are directly related to the infectious and non-infectious complications of the underlying infections by HIV and the immune dysfunction it produces. These clinical manifestations are quite variable, but do follow certain patterns. The infectious agents are those that take advantage of the immune impairment and tend to produce severe, persistent, and relapsing infections. Treatment is frequently complicated by unusual and unanticipated reactions. The challenge of AIDS is to provide appropriate, timely, and non-toxic intervention in a setting that is conducive to recovery.

References

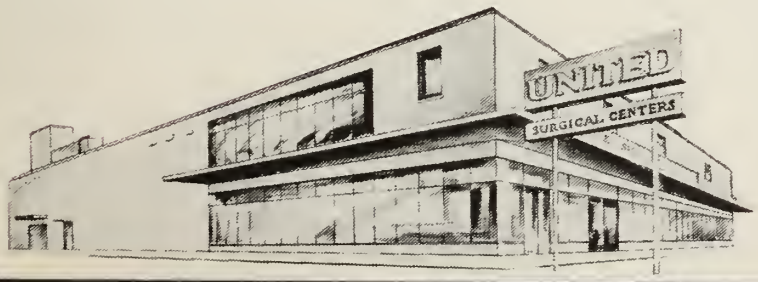
1. Coffin J, Haase A, Levy JA, et al: Human immunodeficiency viruses (letter). Science 232:697, 1986.
2. Melbye M, Biggar RJ, Ebbesen P, et al: Long-term seropositivity for Human T-lymphotropic Virus Type III in homosexual men without the Acquired Immunodeficiency Syndrome: Development of immunologic and clinical abnormalities. Ann Int Med 104:496-500, 1986.
3. Centers for Disease Control: Classification system for Human T-lymphotropic virus type III/lymphadenopathy-associated virus infections. MMWR 35:334-339, 1986.
4. Centers for Disease Control: Kaposi's Sarcoma and Pneumocystis pneumonia among homosexual men — New York City and California. MMWR 25:305-8, 1981.
5. Safai B, Johnson KG, Myskowski PC, et al: The natural history of Kaposi's sarcoma in the Acquired Immunodeficiency Syndrome. Ann Int Med 103:744-749, 1985.
6. Zeigler, JL: AIDS and cancer (abstract). In: Abstracts from International Conference on AIDS, 23-25 June, 1986, Paris, France. Paris: L'Association pour la Recherche sur les Deficits Immunitaires Viro-Induits; 1986:31.
7. Bowen DL, Lane HC, Favci AS: Immunopathogenesis of the Acquired Immunodeficiency Syndrome. Ann Int Med 103:704-709, 1985.
8. Broaddus C, Dake MD, Stulbarg MS, et al: Bronchoalveolar lavage and transbronchial biopsy for the diagnosis of pulmonary

infections in the Acquired Immunodeficiency Syndrome. An Int Med 102:747-752, 1985.
9 Whimbey E, Gold JWM, Polsky B, et al: Bacteremia and fungemia with the Acquired Immunodeficiency Syndrome. Ann Int Med 104:511-514, 1986.
10 Kovacs JA, Kovacs AA, Polis M, et al: Cryptococcosis in the Acquired Immunodeficiency Syndrome. Ann Int Med 103:533-538, 1985.
11 Armstrong D, Gold JWM, Dryjanski J, et al: Treatment of infections in patients with the Acquired Immunodeficiency Syndrome. Ann Int Med 103:738-743, 1985.
12 Curtis J, Goodman P, Hopewell P: Noninvasive tests in the evaluation for P. carinii pneumonia. In: Abstracts from International Conference on AIDS, 23-25 June, 1986, Paris, France. Paris: L'Association pour la Recherche sur les Deficits Immunitaires Viro-Induits: 1986:51.
13 Wharton JM, Coleman DL, Wofsky CB, et al: Trimethoprim-sulfamethoxazole or pentamidine for Pneumocystis carinii pneumonia in the Acquired Immunodeficiency Syndrome. Ann Int Med 105:37-44, 1986.
14 Leong GS, Mills J, Hopewell PC, et al: Dapsone-trimethoprim for Pneumocystis carinii pneumonia in the Acquired Immunodeficiency Syndrome. Ann Int Med 105:45-458, 1986.
15 Brennessel DJ and Goldstein JA: Eflornithine hydrochloride (DFMO) in the therapy of Pneumocystis carinii pneumonia in AIDS (abstract). In: Abstracts from International Conference on AIDS, 23-25, June, 1986, Paris, France. Paris: L'Association pour la Recherche sur les Deficits Immunitaires Viro-Induits: 1986:53.
16 Blumberg RS, Kelsey P, Perrone T, et al: Cytomegalovirus- and Crypotosporidium-associated acalculous gangrenous cholecystitis. Am J Med 76:1118-1123, 1984.
17 Ma P, Villaneuva TG, Kaufman D, et al: Respiratory Cryptosporidiosis in the Acquired Immunune Deficiency Syndrome. JAMA 252:1298-1302, 1984.
18 Centers for Disease Control: Update: Treatment of cryptosporidiosis in patients with Acquired Immunodeficiency Syndrome (AIDS). MMWR 33:117-119, 1984.
19 De la Mont SM, Ho DD, Hirsch MS, et al: Subacute encephalitis of AIDS and correlation with LAV/HTLV-III isolations from neural tissue. In: Abstracts from International Conference on AIDS, 23-25 June, 1986, Paris, France. Paris: L'Association pour la Recherche sur les Deficits Immunitaires Viro-Induits; 1986: 56.
20 Luft BJ, Brooks RG, Conley FK, et al: Toxoplasmic encephalitis in patients with Acquired Immune Deficiency Syndrome. JAMA 252:913-917, 1984.
21 Ho DD, Rota TR, Schooley RT, et al: Isolation of HTLV-III from cerebrospinal fluid and neural tissue of patients with neurologic syndrome related to the Acquired Immunodeficiency Syndrome. N Eng J Med 313:1493-1497, 1985.
22 Holland JC and Tross S: The psychosocial and neuropsychiatric sequelae of the Acquired Immunodeficiency Syndrome and related disorders. Ann Int Med 103:760-764, 1985.
23 Navia BA and Price RW: Clinical features of the AIDS dementia complex. In: Abstracts from International Conference on AIDS, 23-25 June, 1986, Paris, France. Paris: L'Association pour la Recherche sur les Deficits Immunitaires Viro-Induits; 1986:57.
24 Volberding PA: The clincial spectrum of the Acquired Immunodeficiency Syndrome: Implications for comprehensive care. Ann Int Med 103:729-733, 1985.
25 Hawkins CC, Gold JWM, Whimbey E, et al: Mycobacterium avium complex infections in patients with the Acquired Immunodeficiency Syndrome. Ann Int Med 105:184-188, 1986.
26 Fishl MA, Dickinson GM, Sinave C, et al: Salmonella bacteremia as manifestations of Acquired Immunodeficiency Syndrome. Arch Int Med 146:113-115, 1986.
27 Quinnan GV, Jr, Masur H, Rook AH, et al: Herpesvirus infections in the Acquired Immunodeficiency Syndrome. JAMA 252:72-77, 1984.

154 Waterman Street
Providence, RI 02906

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS
The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

There are three ways to bil

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V.	40.-	Billed 9/5/85		100.-
9/30/85		Medicare pmt/adj.		-45.-	-8.-	47.-
10/10/85		patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V.	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/adj		-26.-	-5.-	807.-
1/[illegible]/86		coord. adj.			-3.-	804.-
2/2/86		Medicare pmt/adj		440.-	250.-	114.-

PLEASE PAY LAST AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

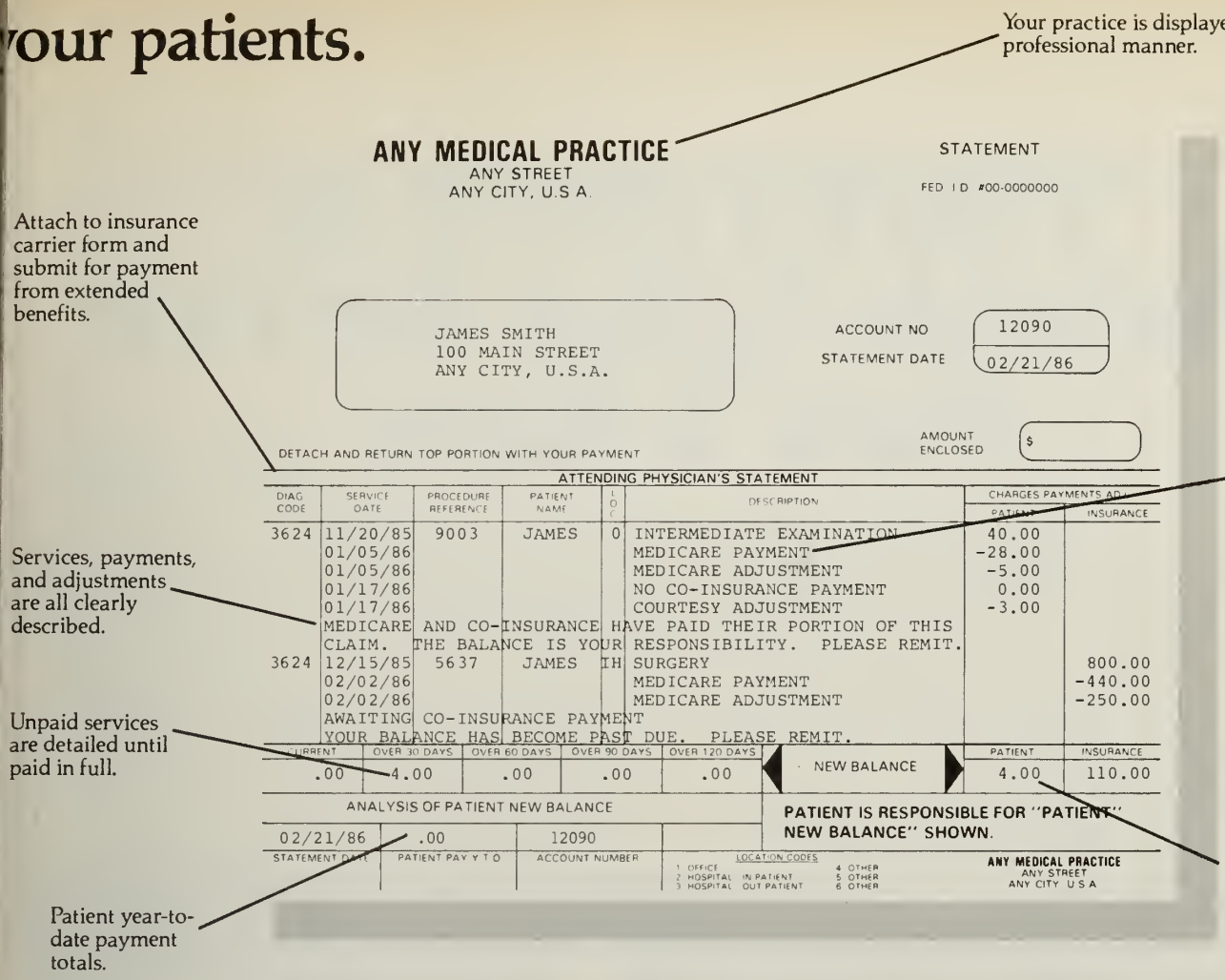
BILLED FROM 1-21-86 DATE 2/21/86
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

your patients.



THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
• Nursing and Convalescent Homes • Shut-ins and Private Home Patients
• Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue	120 Dudley Street	154 Waterman Street	38 Hamlet Avenue
Providence, R.I.	Providence, R.I.	Providence, R.I.	Woonsocket, R.I.
331-3996	331-3996	273-0450	766-4224

Therapeutic Approaches for AIDS and HIV Infection

An Effective Therapy or Preventive Vaccine Are Not Yet Available

Kenneth H. Mayer, MD
Steven M. Opal, MD

With the discovery of the human immunodeficiency virus (HIV, formerly known as HTLV-III/LAV) as the etiologic agent of AIDS,[1,2] it was initially assumed that recent advances in biotechnology and molecular biology would rapidly lead to an effective vaccine against AIDS. In the 3 years since the discovery of HIV, remarkable progress has occurred which has led to a greater understanding of the biology of this virus. The entire genome of the virus has been sequenced and successfully cloned on bacterial plasmids using recombinant DNA technology.[3] Nonetheless, clinically relevant therapies, including antivirals, immunomodulators, as well as a vaccine have not yet been implemented. Much exciting laboratory work has led to the development of several promising antiviral and immunoadjuvant therapies, but clinical trials up until now have not demonstrated any agent that irreversibly reconstitutes the infected immune system or eliminates the retrovirus, which can remain dormant for years. With the establishment of a national program of treatment centers, the slow process of the clinical evaluation of newer drugs will, it is hoped, be greatly speeded up. The prospects for a vaccine in the near future appear to be unlikely, since several laboratory and clinical concerns must be resolved by virologists, molecular biologists, immunologists, and public health officials before effective immunization against AIDS becomes a reality. This paper will review the current research efforts directed towards understanding how to prevent or ameliorate the sequelae of HIV infection.

From the Division of Infectious Diseases, Memorial Hospital, Pawtucket, and Brown University, Providence, RI

Dr Kenneth H. Mayer is Chief of the Infectious Disease Division and Dr. Steven M. Opal is an Infectious Disease Specialist at Memorial Hospital, Pawtucket, RI 02860

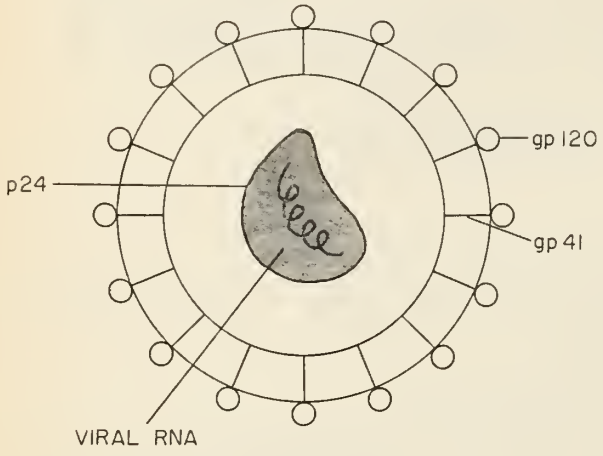
Antiviral Strategies

Successful therapy or prevention of HIV infection has focused on defining virus-specific sites of activity that may be amenable to intervention (Figs 1 and 2; Table 1). The attachment of the viral envelope glycoprotein (GP120) to the T4 lymphocyte receptor is a necessary and specific condition for subsequent HIV infection[4,5] and hence the focus of many vaccination strategies. After attachment and penetration, the virus is uncoated in the cytoplasm, and the reverse transcriptase enzyme encoded by HIV transcribes the viral RNA, producing proviral DNA copies. Some of these are integrated into the chromosome of the host cells and others remain free in the cytoplasm.[6] The provirus is subsequently transcribed, and its messenger RNAs are modified, resulting in the translation into viral-specific proteins. Several of these proteins are precursors which undergo subsequent cleavage to produce biologically active molecules. Thus, once an HIV virion enters a susceptible target cell, which may include T and B infected lymphocytes, monocytes, and possibly endothelial cells,[7] it can direct the cell's genes to produce injurious intracellular proteins as well as multiple HIV copies which can be released to infect other cells. Any of these steps may provide adequate targets for antiviral therapy.

Antireverse Transcriptase Agents

Because the most virus-specific step in the replication cycle of HIV and other retroviruses is reverse transcription, it has been a major focus of therapeutic strategies. Reverse transcriptase inhibitors may act in a variety of ways. Ribavirin is a substrate analog,[9] while single-stranded polyribonucleotides, oligonucleotides, and modified

Fig 1



gp120 = ENVELOPE GLYCOPROTEIN
gp 41 = TRANSMEMBRANE GLYCOPROTEIN
p24 = CORE PROTEIN
VIRAL RNA CONTAINS REVERSE TRANSCRIPTASE GENE

polynucleotides such as azidothymidine, 2′-deoxyadenosine, and 2′deoxycytidine are template analogs which compete for template/primer binding sites on the enzyme with unaltered nucleotides.[10] Pyrophospate analogs, such as trisodium-phosphonoformate (PFA) act as noncompetitive inhibitors of both the substrates and templates of reverse transcriptase.[11] Suramin[12] and HPA-23[13] are polyanionic substances that compete with the template/primer. Other compounds which interfere with reverse transcription in other ways, such as enzymatic chelation, are under active investigation.[7]

The clinical efficacy of antireverse transcriptase agents has not yet been fully established, but several compounds show promise. Some, but not all, of the 19 subjects with a diagnosis of AIDS who underwent a 6-week trial of azidothymidine regained skin test reactivity, enhanced natural killer cell function, and were mononuclear cell culture negative for HIV.[10] However, the drug affects all blood cell lines, often resulting in megaloblastic anemic and leukopenia at therapeutic doses. Since the drug is available in oral and intravenous preparations, and is generally well-tol-

Fig 2

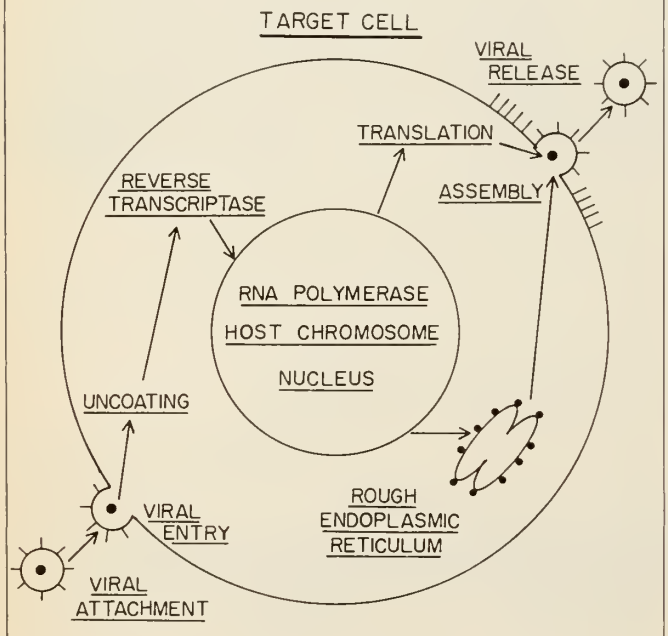


Table 1 — Sites of Action of Specific Interventions

Viral Attachment
1. Vaccine
2. Hyperimmune globulin
3. AL-721 (?)

Reverse Transcriptase
1. Antimonitungstate (HPA-23)
2. Azidothymidine
3. Ansamycin
4. Ribavirin
5. Suramin
6. Trisodium phosphonoformate (PFA)
7. 2′-Dideoxyadenosine
8. 2′-Dideoxycytidine
9. Interferon?

Translation, Assembly, Release
1. Interferon
2. Al-721 (?)
3. Monoclonal antibodies to infected cells
4. Sensitized T cells

Immunomodulators
1. Interferon
2. Interleukin-2
3. Isoprinosine
4. Colony stimulating factor
5. Thymic hormones
6. Opiate antagonists
7. Cyclosporine
8. Lymphokines, and other soluable mediators
9. Plasmapheresis

erated, it is the focus of much optimism. However, HIV may persist integrated in the host genome as a provirus indefinitely. Thus, caution must be maintained until subjects have been monitored after therapy for months, if not years. Other potent congeners of azidothymidine, 2′-dideoxycytidine and 2′-dideoxyadenosine have shown excellent antiviral activity in the test tube, and will soon undergo clinical trials.[14]

Ribavirin has been an effective reverse transcriptase inhibitor *in vitro*, and early clinical data have shown *in vivo* viral inhibition and clinical improvement in some of the subjects' studies.[15] Phosphonoformate (PFA, Foscarnet®) therapy resulted in improvements in delayed hypersensitivity and HIV suppression in several subjects; but in about half of them the virus was soon recovered after the cessation of therapy.[16] Side effects of PFA treatment included headaches, axillary thrombosis, and anemia. The toxic side effects of both suramin[17] and HPA-23[18] have been severe enough to raise questions regarding their utility in the management of HIV infection. Suramin has been associated with fevers, rashes, hepato- and nephrotoxicity, while the major problem for patients who received HPA-23 was thrombocytopenia. HIV was frequently cultured from mononuclear cells from subjects who received these drugs once therapy was stopped.

Immunomodulators and Other Anti-HIV Therapies

Before the elucidation of HIV as the etilogic agent of AIDS, early therapeutic attempts focus on immunologic reconstitution with a variety of drugs that specifically and nonspecifically bolster the immune system. A major problem with the immunomodulators is that by enhancing the number of T helper/inducer lymphocytes after the initial HIV infection, the only effect observed may be an increase in the number of infected cells without immunologic improvement. Interferons are a class of proteins produced in response to viral or other antigenic challenges with multiple actions against a wide range of viruses. Recombinant alpha interferon significantly inhibits HIV *in vitro* at several sites of viral activity.[19] Treatment with recombinant alpha interferon has resulted in significant clinical responses in some of the subjects with Kaposi's Sarcoma,[20] but has not been effective in facilitating immune enhancement and retarding clinical progression among patients with opportunistic infections.

Interleukin-2 is a T-cell growth factor which has been shown to enhance *in vitro* killer cell activity in persons with AIDS,[21] but does not stop viral replication. Hence, its use as a single agent is limited. However, it may be useful in future combinations with antiviral drugs. Isoprinosine is a nucleoside derivative which has been shown to enhance T-cell function including proliferation responses to mitogens in patients with AIDS-related symptoms, but not in persons with AIDS.[22] Several individuals with identical twins have undergone complete immune reconstitution with bone marrow transplants.[21] The only person who has survived this complicated process for more than six months received concurrent low dose suramin.[23] Given the risks associated with heterologous transplants, particularly in HIV-infected persons, this procedure will probably be of limited utility. However, it underscores the perception that viral eradication as well as immune reconstitution will be necessary to manage persons who have longstanding HIV infection.

Other immunological approaches that have not been clinically evaluted include the use of thymic hormones to facilitate T-cell differentiation,[21] and colony stimulating factor which acts upon hematopoietic precursors (Doctor J. E. Groopman, personal communication). Since endorphins have been shown to diminish T helper cell function, there is hope that opiate antagonists such as naltrexone may be immunorestorative. The presence of immune dysregulation with hypergammaglobulinemia and autoimmune phenomena[21] has led some to postulate that immunosuppressive therapy may actually have a role in the management of HIV disease.[24] Experience with cyclosporin and monoclonal antibodies against T suppressor lymphocytes has not substantiated this approach as monotherapy and continues to raise concerns among cautious investigators who feel that HIV-infected individuals are already sufficiently immunosuppressed.

Therapeutic Considerations

Current anti-HIV treatment protocols are still in fairly rudimentary stages of investigation. There are several promising compounds with specific anti-viral and immunorestorative potential, but since the pathophysiologic understanding of the natural history of HIV infection is not complete, basic questions regarding therapy persist. Should individuals be treated as soon as they are seroconverted, or only after initial signs of immunologic impairment supervene? How long should therapy continue? Since the virus may remain latent indefinitely, one may argue that chronic lifelong viral suppression will be necessary. What

are the salient parameters for monitoring therapeutic efficacy? Are clinical symptoms, lymphocyte subpopulation number and function, or viral culture data the most relevant indicators of clinical response?

The investigation of any new drug may raise similar questions as well as others regarding toxic-therapeutic ratio, pharmacokinetics, rates of absorption, and routes of excretion. The fact that HIV readily infects the central nervous system and tissue macrophages may have major bearing on the answers.[23] Lastly, a major therapeutic question in the next few years will be whether combination therapy is indicated. This will raise difficult protocol questions since two drugs that are independently ineffective may have a synergistic effect, and two drugs that are independently effective may be antagonistic together. Whether the combination of antiviral and immunomodulating compounds is better than two antivirals that act at different sites remains to be seen. Since the answers to these questions may take much time, clinicians and bench researchers must be cautious in making public pronouncements regarding therapeutic efficacy.

Viral Antigens and Vaccine Strategies

The virus synthesizes at least four important gene products that are necessary for viral replication and pathogenicity (Fig 2). These genes include: 1) the *gag* gene, which synthesizes the core structure of the virus, 2) the *pol* gene, which synthesizes reverse transcriptase, 3) the *tat* gene, which mediates transactivating transcriptional function, 4) the *env* gene, which synthesizes the envelope proteins.[25] The envelope protein is transcribed as a single polypeptide which is subsequently glycosylated and has a molecular weight of 160 kilodaltons. The protein is subsequently hydrolyzed giving rise to gp120 at the amino-terminus and gp41 at the carboxy-terminus. The gp120 serves as the major external structural protein of the virus, while gp41 functions as a transmembrane protein attaching the envelope to the virus core. The structural glycoprotein of the virus envelope is the most attractive candidate for subunit virus vaccine development. The envelope protein is immunogenic, exposed to an exterior surface of the virus, and probably serves as an attachment site for susceptible human cell lines.[26] A subunit vaccine using envelope antigens has recently been developed against feline leukemia virus, a retrovirus related to HIV. This demonstrates the potential utility of this vaccine strategy in the development of vaccine against the AIDS virus.[27]

Technical advances in defining the virus structure of HIV would appear to make a subunit vaccine feasible. However, several aspects of the basic behavior of this virus make vaccine development more difficult. Investigation into the genetic stability of HIV has demonstrated that the virus is quite variable in its genetic makeup. Up to 10 per cent of the entire viral genome may differ between one human isolate to another.[28] There is marked variation in the genetic makeup of virus isolates from different geographic regions. Despite this variation, infected individuals express only one or perhaps two different virus types at any given time. Single human isolates appear to be quite stable when cultured for extended periods of time in cell culture systems.

The frequency with which viral strains undergo genetic rearrangement within the human host is not yet known. Since there are multiple variants of the structural proteins which form the dominant epitopes of the virus envelope, it is likely that multiple serotypes of the virus exist in nature. This finding has disturbing implications for vaccine development. It may be necessary to develop a polyvalent vaccine against multiple serotypes of the virus. Alternatively, conserved regions within multiple strains of HIV could be isolated and used as a vaccine. This may be sufficient to provide cross protection against a broad range of structurally distinct virus envelopes.[29]

Using a computer-generated model of the virus envelope based upon the nucleotide sequence of the viral genome, certain sequences of amino acids appear to be highly conserved. These conserved regions of the envelope protein are hydrophilic and appear to be expressed on the exterior surface of the virus envelope. These regions may be conserved since they serve a vital function in virus structure or may be attachment sites to human cells. Synthetic peptides have been derived from these conserved regions and these peptides have been shown to generate antibodies which recognize the native envelope glycoprotein of HIV.[30] Detailed molecular analysis of the structure of the virus coat may reveal highly conserved regions which stimulate the formation of neutralizing antibody. Although the potential for vaccine development against AIDS still exists, it appears to be a more complex problem than was initially suspected.

A number of options are available to isolate relevant viral antigens for vaccine development. Live attenuated retrovirus vaccines will almost certainly be unacceptable for human use. These

viruses have the potential for genomic reassortment, and viral integration into human DNA, and are potentially oncogenic. Even killed virus vaccines would be difficult to license for human use owing to safety concerns over incomplete inactivation and the possibility of vaccine-related disease. The most likely system for generating viral antigens for vaccine development will be the use of recombinant nucleic acid technology. Subunit viral antigens could be generated using cloning vectors in prokaryotic or eukaryotic cell systems.[31]

The Molecular Biology of Vaccine Development Against AIDS

Two major problems face the molecular biologist attempting to use recombinant DNA technology to construct a vaccine against the human immunodeficiency virus. First, the principal antigenic constituents of the virus envelope (immunodominant epitopes) must be identified. This epitope (or epitopes) should be capable of generating an antibody which recognizes virus strains isolated from different geographic areas. Second, the genetic material which synthesizes this epitope must be cloned in a vector system which expresses virus antigens in a highly immunogenic form.[32]

Detailed analysis of the structural components of the virus envelope reveal extensive glycosylation. This present great difficulties for the molecular cloning of this viral structure. Post-translational modification of polypeptides by glycosylation significantly alters the tertiary structure of the final protein. This could affect the antigenic nature of the envelope protein. Molecular cloning in bacterial or yeast systems results reproducibly in exact replicas of the amino acid sequence of a given gene. However, neither bacterial nor yeast cloning vectors glycosylate proteins effectively which may lead to a less immunogenic envelope antigen. It may be necessary to clone the genes for viral antigens in mammalian vector systems. The use of mammalian cell systems as cloning vectors is considerably more difficult and costly, yet it may prove necessary to assure a highly immunogenic, glycosylated product which mimics the virus envelope itself. Another possible expression vector is the use of a hybrid vaccinia virus system. Vaccinia, the virus found in the smallpox vaccination, could be genetically engineered to express HIV envelope antigens. Such a system could potentially lead to a safe and economically feasible vaccine candidate and is under investigation.[33]

Immunologic Considerations in the Development of an AIDS Vaccine

Assuming that the relevant viral epitopes can be identified and manufactured by an acceptable cloning system, other problems arise which could jeopardize the development of an effective vaccine. A troublesome finding, which must be considered in future vaccine strategies, is the lack of protective immunity induced by natural virus infection itself. Serum antibody is occasionally isolated from patients infected with HIV which will neutralize the ability of HIV to infect susceptible cell lines *in vitro*.[34,35] Antibody titers appear to be low and have not been shown to protect human victims from subsequent infection. It may be necessary to add immunostimulants to vaccine preparations to maximize the immune response to viral antigens. Immunopotentiation can be accomplished by various methods, but this may further complicate efforts to produce a safe and effective vaccine.

Another concern is the potential necessity of providing mucosal immunity as well as humoral immunity. Since the virus is presumably infectious once deposited on mucous membranes, local protective antibodies in the genital and rectal mucosa prior to exposure to HIV may be necessary. If the virus gains access to susceptible cells (such as lymphocytes or macrophages) at the mucosal level, prevention of widespread infection of the host despite adequate serum antibody levels may prove to be difficult.

Another difficulty is the limited availability of suitable animal models for the study of the protective efficacy of candidate vaccine. The chimpanzee model appears to be the most appropriate animal model to study human disease related to HIV.[36] Studies with vaccinated animals following intravenous challenge with an infectious dose of HIV will prove invaluable in development of a human vaccine. However, demonstrable protection against intravenous challenge may not ensure protection against an infectious dose of HIV through sexual secretions. Since homosexual and heterosexual transmission remains the principal means of spread of the AIDS virus, providing vaccine efficacy against this sexually transmitted disease will be important.

Clinical Immunology and Public Health Concerns Related to an AIDS Vaccine

Assuming that a vaccine is developed which offers protection in experimental animals, a number of other difficulties remain before vaccination of the public becomes feasible. Safety and

efficacy trials must be conducted with measurement of protective neutralizing antibody titers in vaccine recipients. It will be difficult, if not impossible, to determine the minimum antibody titer which will protect the human host from infection with HIV. It would certainly be unethical to challenge vaccine recipients with viable HIV. This information therefore must be extrapolated from animal studies. If safety and efficacy can be assured, field trials will then be conducted. Major questions remain even at this stage of vaccine development. Will the vaccine work in actual field conditions? Will the vaccine be efficacious against parenteral as well as sexual transmission of HIV? How uniform will the antibody response be among recipients of the vaccine? What is the most effective means of vaccinating individuals? How high must neutralizing antibody titers be to offer protection, and how long does this protection last? How frequently will booster immunizations be required? The answers to these questions will not be available immediately. A prolonged concerted effort by clinical investigators will be required before a rational vaccine program is developed.

Public Health Issues and Society's Response to a Candidate AIDS Vaccine

A final concern which may impede effective vaccination against AIDS is the public's response to a newly developed AIDS vaccine. It would be desirable to target a vaccine at members of high risk groups. However, it is unlikely that administration of this vaccine by sexually transmitted disease clinics or methadone maintenance clinics would be effective. The prevalence of HIV infection in patients who are seen in such clinics is already substantial. As the prevalence of HIV increases in the American population, heterosexual transmission will become an increasingly important means of transmission of this virus. Targeting vaccine strategies at intravenous drug abuser and gay men may miss a substantial number of individuals who will be exposed to this virus in the near future. The epidemiology of HIV emphasizes the need to administer the vaccine at an early age. The vaccine could be added to vaccination programs within the public school systems. It may be necessary to provide immunizations to the entire population to interrupt effectively the transmission of HIV. This will prove to be expensive. Safety concerns will be magnified when this vaccine is administered to millions of people. How much money is the American public willing to spend and how much risk is it willing to take in accepting a vaccine of unproven efficacy and uncertain safety? There may be significant segments of our society who will oppose this vaccine for religious, ethical, or economic reasons. Medical/legal concerns about liability claims from adverse vaccine reactions will probably require government intervention before pharmaceutical companies will be willing to manufacture a candidate vaccine.[31]

Although the notion of developing an AIDS vaccine is appealing, serious scientific and public health issues must be solved before a viable vaccine strategy is possible. Even if an effective vaccine were immediately available, it would be of little benefit for the more than one million Americans who are currently infected with the virus. Antiviral agents, immunostimulatory compounds, infection control policies, and educational programs must be developed along with an AIDS vaccine program ultimately to end the current AIDS epidemic.

References

1. Gallo RC, Sarin PS, Gelmann EP, et al: Isolation of human T cell leukemia virus in acquired immunodeficiency syndrome (AIDS). Science 220:865-868, 1983.
2. Barre-Sinoussi F, Chermann C, Rey F, et al: Isolation of T-lymphotropic retrovirus from a patient at risk for acquired immunodeficiency syndrome (AIDS). Science 220:868-871, 1983.
3. Ratner L, Haseltine W, Patarca R, et al: Complete nucleotide sequence of AIDS virus, HTLV-III. Nature 313:277-284, 1985.
4. Klatzmann D, Champagne E, Chamaret S, et al: T-lymphocyte T4 molecule behaves as the receptor for human retrovirus LAV. Nature 312:767-768, 1984.
5. Richardson CD, Scheid A, Choppin PW: Specific inhibition of paramyxovirus and myxovirus replication by oligopeptides with amino acid sequences similar to those at the N-termini of the F_1 or HA_2 viral polypeptides. Virology 105:205-222, 1980.
6. Montagnier L: Lymphadenopathy-associated virus: From molecular biology to pathogenicity. Ann Intern Med 103:689-693, 1985.
7. Hirsch MS, Kaplan JC: Prospects of therapy for infections with human T-lymphotropic virus type III. Ann Intern Med 103:750-755, 1985.
8. Gallo RC, Wong-Staal F: A human T-lymphotropic retrovirus (HTLV-III) as the cause of the acquired immunodeficiency syndrome. Ann Intern Med 103:679-689, 1985.
9. McCormick JB, Getchell JP, Mitchell SW, Hicks DR: Ribavirin suppresses replication of lymphadenopathy-associated virus in cultures of human adult T lymphocytes. Lancet 2:1367-1369, 1984.
10. Yarchoan R, Weinhold KJ, Lyerly HK, Gelmann G, Blum RM, Shearer GM, Mitsuya H, Collins JM, Myers CE, Klecker RW, Markham PD, Durack DT, Lehrman SN, Barry DW, Fischl MA, Gallo RC, Bolognesi DP, Broder S: Administration of 3′-azido-3′deoxythymidine, an inhibitor of HTLV-III/LAV replication, to patients with AIDS or AIDS-related complex. Lancet 3:575-582, 1986.
11. Sandstrom EG, Kaplan JC, Byington RE, Hirsch MS: Inhibition of human T-cell lymphotropic virus type III in vitro by phosphonoformate. Lancet 1:1480-1482, 1985.
12. Broder S, Collins JM, Markham PD, Redfield RR, Hoth DF, Groopman JE, Gallo RC, Yarchoan R, Lane HC, Klecker RW, Mitsuya H, Gelmann E, Resnick L, Myers CE, Fauci AS: Effects

of suramin on HTLV-III/LAV infection presenting as Kaposi's sarcoma or AIDS-related complex: clinical pharmacology and suppression of virus replication in vivo. Lancet 9:627-630, 1985.
13 Des Jarlais DC, Friedman SR, Hopkins W: Risk reduction for the acquired immodeficiency syndrome among intravenous drug users. Ann Intern Med 103:755-759, 1985.
14 Broder S: Inhibition of the in vitro infectivity and cytopathic effect of HTLV-III/LAV by purines and pyrimidines with the ribose moiety in a 2′, 3-′dideoxy-configuration. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
15 Crumpacker CS, Bubley G, Hussey S, Schnipper L, Heagy W, Finberg R, et al: Evaluation of oral ribavirin therapy on immunologic and viral parameters in AIDS and ARC. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
16 Farthing CF, Dalgleish AG, Clark AL, Chanas A, McClure M, Gazzard GG: Pilot study on the treatment of AIDS and ARC patients with intravenous Foscarnet. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
17 Cheson BD, Levine A, Mildvan D, Kaplan L, Rios A, Wolfe P, et al: Suramin therapy in AIDS and related diseases: initial report of the U.S. suramin working group. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
18 Dormont D, Maillet T, DiMaria H, Gardere M, Barre-Sinoussi FC, Chermann JC: Virologic and immunologic follow-up of 15 patients with AIDS or AIDS related complex, and 4 LAV/HTLV-III seropositive patients treated with daily IV doses of HPA during 4 to 15 months. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
19 Ho DD, Hartshorn KL, Rota TR, et al. Recombinant human interferon alfa-A suppresses HTLV-III replication in vitro. Lancet 1:602-604, 1985.
20 Krown SE, Real FX, Gold JWM, Vadhan-Raj S, Lester TJ, Armstrong D, Oettgen HF: Therapeutic trials of interferon alfa-2a (IFN-alpha2a) in AIDS-related Kaposi's sarcoma (KS/AIDS). Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
21 Lane HC, Fauci AS: Immunologic reconstitution in the acquired immunodeficiency syndrome. Ann Intern Med 103:714-718, 1985.
22 Grieco MH, Reddy MM, Manvar D, Ahuja KK, Moriarty ML: In vivo immunomodulation by isoprinosine in patients with acquired immunodeficiency syndrome and related complexes. Ann Intern Med 101:206-207, 1984.
23 Fauci AS, Lane CH: Therapeutic approaches to the underlying immune defect in patients with AIDS. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
24 Klatzmann D, Gluckman JC: The pathophysiology of LAV/HTLV-III: a complex pathway of host-virus interaction. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
25 Essex M, Allan J, Kanki P, et al: Antigens of human T-lymphotropic virus type III/lymphadenopathy-associated virus. Ann Intern Med 103:700-703, 1985.
26 Barin F, McLane MF, Allan JS, et al: Virus envelope protein of human T cell leukemia virus type III (HTVL-III) represents major target antigen for antibodies in AIDS patients. Science 228:1094-1096, 1985.
27 Lewis MG, Mathes LE, Olsen RG: Protection against feline leukemia by vaccination with a subunit vaccine. Infect Immun 34:888-894, 1981.
28 Wong-Staal F, Shaw GM, Hahn BH, et al: Genomic diversity of human T lymphotropic virus type III (HTLV-III). Science 229:759-762, 1985.
29 Groopman JE: Laying the groundwork for neutralizing AIDS-linked virus. Nature 316:12, 1985.
30 Kennedy RC, Henkel RD, Pauletti D, et al: Antiserum to a synthetic peptide recognized as the HTLV-III envelope glycoprotein. Science 231:1556-1559, 1986.
31 Francis DP, Patricciani JC: The prospects for and pathways toward a vaccine for AIDS. N Engl J Med 313:1586-1590, 1985.
32 Crowl R, Ganguley K, Gordon M, et al: HTLV-III *env* gene products synthesized in *E. coli* are recognized by antibodies present in the sera of AIDS patients. Cell 41:959-968, 1985.
33 Hu SL, Kosowski SG, Purchio AF, Dalrymple JM: Expression of AIDS virus envelope gene in recombinant vaccinia virus. Abstract of the Second International Conference on AIDS, Paris, June 23-25, 1986.
34 Weiss RA, Clapham PR, Cheingsong-Popov R, et al: Neutralization of human T lymphotropic virus type III by sera of AIDS and AIDS-risk patients. Nature 316:69-72, 1985.
35 Robert-Guroff M, Brown M, Gallo RC: HTLV-III-neutralizing antibodies in patients with AIDS and AIDS-related complex. Nature 316:72-74, 1985.
36 Alter HJ, Eichberg JW, Masur H, et al: Transmission of HTLV-III infection from human plasmid to chimpanzees: an animal model for AIDS. Science 226:549-552, 1984.

Rhode Island

ADVERSE DRUG REACTION
Reporting Project

SUSPECT A SERIOUS OR UNEXPECTED

ADVERSE DRUG REACTION?

Please Report It.

SUSPECTED ADVERSE REACTION REPORT (For All Drugs and Biologics)

IMPORTANT: SUBMISSION OF A REPORT DOES NOT NECESSARILY CONSTITUTE AN ADMISSION THAT THE DRUG CAUSED THE ADVERSE REACTION

PATIENT INITIALS (Optional)	AGE (Years)	SEX	DATE OF REACTION ONSET
A.D.R.	54	☑ MALE ☐ FEMALE	12 Oct. 1986

DESCRIBE REACTION(S) (Give signs, symptoms, diagnoses, course and lab findings)

JAUNDICE

CHECK ALL APPROPRIATE TO REACTION
- ☐ DIED
- ☑ TREATED WITH Rx DRUG
- ☑ INPATIENT HOSPITALIZATION
- ☐ SEVERE OR PERMANENT DISABILITY
- ☐ EMERGENCY ROOM TREATMENT
- ☐ TREATMENT IN PHYSICIAN OFFICE
- ☐ NONE OF THE ABOVE

SUSPECTED DRUG(S) (Trade Name is preferred. If a generic product, give manufacturer. Indicate Lot No. for vaccines, biologics)

[redacted]

REASON FOR USE OF DRUG(S)	ROUTE	TOTAL DAILY DOSE	DATES OF ADMINISTRATION
HYPERTENSION	P.O.	100mg.	9 Sept.- 12 Oct. '86

OTHER DRUGS TAKEN CONCOMITANTLY (Exclude those used to treat reaction)

None

OTHER RELEVANT HISTORY (e.g. Concomitant Diagnoses, Pregnancy, etc.)

None

PHYSICIAN NAME AND TELEPHONE NUMBER

J. Doe, M.D. 277-2550

Confidential

ALSO REPORTED TO MANUFACTURER ☑ YES ☐ NO

For report cards, guidelines and information contact Dr. S. Rosenbaum, 277-2550

A pilot project of the Rhode Island Department of Health
sponsored by the U.S. Food and Drug Administration

The Epidemiology and Control of AIDS and HIV Infection in Rhode Island

Alternative Testing Sites and Community Cooperative Efforts Are Features of Control Strategy

Richard A. Keenlyside, MD
L. Dondero
M. Corkery, RN
A. Johnson, RN

Over 22,000 cases of the acquired immune deficiency syndrome (AIDS) have now been reported in the United States since the syndrome was first described in the summer of 1981. The syndrome has been reported from over 100 countries and four continents, and is a profoundly serious problem in Africa where incidence rates may approach those of New York and San Francisco (600-700 per million).

Since the beginning of the epidemic in the United States, new cases have been reported at an alarming rate (doubling approximately every twelve to fourteen months), and the epidemiological characteristics of the disease have been remarkably constant.

Most adult cases have occurred in homosexual/bisexual men (74 per cent) and the remainder have been in intravenous drug abusers (17 per cent), persons with hemophilia (1 per cent), blood transfusion recipients (2 per cent), and (4 per cent) heterosexual contacts of persons in high-risk groups. Among the more than 300 cases reported in children, 79 per cent were born to parents with AIDS or in high-risk groups. Three per cent of cases in both adults and children have had no risk factor identified.

Richard A. Keenlyside, MD is Chief of the Division of Disease Control, Rhode Island Department of Health, and Clinical Assistant Professor of Community Health at Brown University.

L. Dondero, M. Corkery, RN, and A. Johnson, RN, are staff members in the Division of Disease Control, Rhode Island Department of Health.

It has now been firmly established that the virus is transmitted via intimate sexual contact, sharing of needles among drug abusers, and from an infected mother to her children during the perinatal period. Spread of the infection by other modes of contact has not been documented and most likely does not occur.

The causative agent, a human retrovirus, was identified in 1983. This was first known as the Human T Lymphotrophic Virus Type III/Lymphadenopathy Associated Virus (HTLV-III/LAV), but has since been renamed the human immunodeficiency virus (HIV).

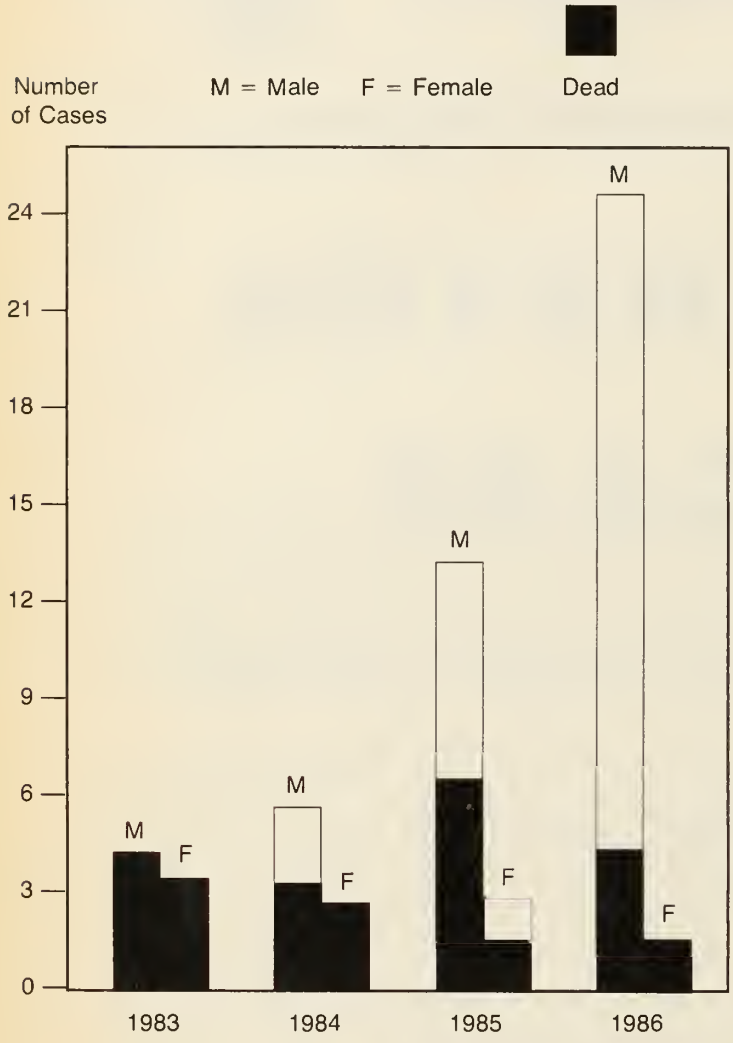
Serological studies have shown that the infection is widespread among high-risk groups. Asymptomatic infection is common, but the incubation period before the onset of symptoms may be as long as five years. It has been estimated that between one and two million Americans may be infected with the virus, and over the next five years approximately 30 percent of these will develop AIDS. In 1991 alone more than 145,000 persons with AIDS may require medical care, and 54,000 will die.

These alarming statistics have already been reflected in an increase in reported cases in Rhode Island, and an increased demand on state agencies and health care providers for services. This paper outlines the epidemiology of reported AIDS cases in Rhode Island over the past three years, and the Health Department Strategy for controlling the epidemic.

Cases of AIDS Reported in Rhode Island

The syndrome of AIDS was first made reportable in Rhode Island in August, 1983. By August

Fig 1. Cases of the Acquired Immunodeficiency Syndrome (AIDS) Reported in Rhode Island, August 22, 1983-August 12, 1986.



Reported Cases

		R.I. (%)
Homosexual/Bisexual Males	29	56%
Intravenous Drug Abusers	20	38%
Transfusion Associated	2	4%
Child of High-Risk Group Member	1	2%
Other (Hemophilia, Heterosexual, Unknown, Other)	0	0
	52	100%

12, 1986, 52 cases (44 males and 8 females) had been reported (7 in 1983, 7 in 1984, 14 in 1985 and 24 so far in 1986) (Figure 1). Active surveillance by the AIDS control activity has identified an additional 32 cases of AIDS-Related Complex (ARC), an illness characterized by fever, weight loss, and lymphadenopathy, but without the opportunistic infections and neoplasms that are seen in AIDS. Eight of the reported cases in Rhode Island residents were diagnosed in other states. Twenty-six (50 per cent) of the 52 cases have died.

The cumulative incidence of AIDS in Rhode Island is now approximately 54 per million population, which is similar to the rates estimated for elsewhere in the United States outside of high-incidence areas. Rates of between 70 and 76 per million have been reported in Connecticut, Massachusetts, and upstate New York. These are much lower than the rates of more than 300 per million occurring in Boston and 600 per million in New York City.

Twenty-nine (56 per cent) of the reported cases in Rhode Island have been in homosexual or bisexual men and 20 (30 per cent) in intravenous drug abusers: Two (4 per cent) were related to blood transfusion, and one occurred in a child of a woman in a high-risk group.

Although increasing numbers of cases are now being reported in homosexual men, the percentage of cases reported among intravenous drug abusers in Rhode Island (30 per cent) seems alarmingly high and is much greater than the national rate of 17 per cent. The reasons for this are not clear. There may be a higher prevalence of infection among intravenous drug abusers in the state, but homosexual men may be underrepresented among the cases, since there is some evidence that they may prefer to obtain medical care out of the state. We have insufficient information about the behavioral characteristics of the two high-risk groups to draw firm conclusions at this time.

Studies of intravenous drug abusers entering the single methadone maintenance program in Rhode Island have revealed a prevalence of infection of approximately 20 per cent among those tested (personal communication, A. Amicarelli). The problem warrants urgent intervention, since infection and death from AIDS following needle sharing has been documented among several drug abusers in the state. For example, among a group of seven needle-sharing drug abusers identified over the past two years, five have developed AIDS, four are dead and two of the survivors have ARC.

Predictably AIDS and HIV infection have been identified among inmates of the Rhode Island State Adult Correctional Institution (ACI), which has over 1,500 inmates in seven facilities. It has been estimated that between 30 and 40 per cent

of these cases have a history of intravenous drug abuse. Since reporting began, one case of AIDS, one case of ARC, and five other infections with HIV have been identified in inmates of the Adult Correctional Institution in Cranston, Rhode Island.

Screening for Virus in Donated Blood

All blood donated in Rhode Island is processed by the Rhode Island Blood Center. Since 1983 all donors from high-risk groups have been requested to defer donation or have their blood withdrawn after donation.

In March 1985 an enzyme-linked immunosorbent assay test (ELISA) that detects antibodies to HIV in blood was licensed in the United States. A repeatedly positive ELISA test, when confirmed by Western blot analysis of viral proteins, confirms that the individual has been infected with the virus. Since March 1985 all blood donated in Rhode Island has been tested for the virus. By August 1986 almost 78,000 units had been tested and 15 (0.02 per cent) were found repeatedly to be reactive. Thirteen of these infected donors have been contacted: Nine were from high risk-groups; four had no identifiable risk factors, and the remaining two were either untraced or unresponsive to requests for counseling.

HIV Antibody Testing of Specimens Submitted to the Rhode Island State Laboratory

In June 1985 the state laboratory offered testing for HIV antibody on specimens submitted routinely by private physicians.

Personal identifying information is not required on the serology form for this test. A code number known to the attending physician is acceptable. Physicians are notified of the test result by telephone by the Division of Disease Control and later in writing. No communications are issued by the laboratory staff.

We recommend strongly that all persons tested be counseled about the value of the test before it is carried out.

All persons who are tested should be given post-test counseling and health education by their health care provider regardless of the risk group of the patient and the test result. This should include specific information about risk-reduction measures the patient should take to avoid infection and prevent transmission. Guidelines for testing and counseling patients are included in a booklet entitled "AIDS: A management guide for health care providers in Rhode Island" available from the Division of Disease Control.

Table 1. Results of Testing for HIV Virus on Blood Specimens Submitted to Rhode Island State Laboratory June 1985 to August 1986

Specimen Submitted By:	N	HIV Positive*	%
Hospitals/Laboratories	512	106	20.7
Private Physicians	431	20	4.6
Health Maintenance Organizations	32	6	18.7
Other Agencies (Clinics, Health Centers, Colleges, Rehabilitation Centers, etc.)	179	16	8.9
Total	1154	48	12.8

*By repeat ELISA and Western blot testing.

Between June 1985 and August 12, 1986, 1154 specimens submitted by health care providers were tested at the state laboratory. The results are given in Table 1 according to the origin of the specimens.

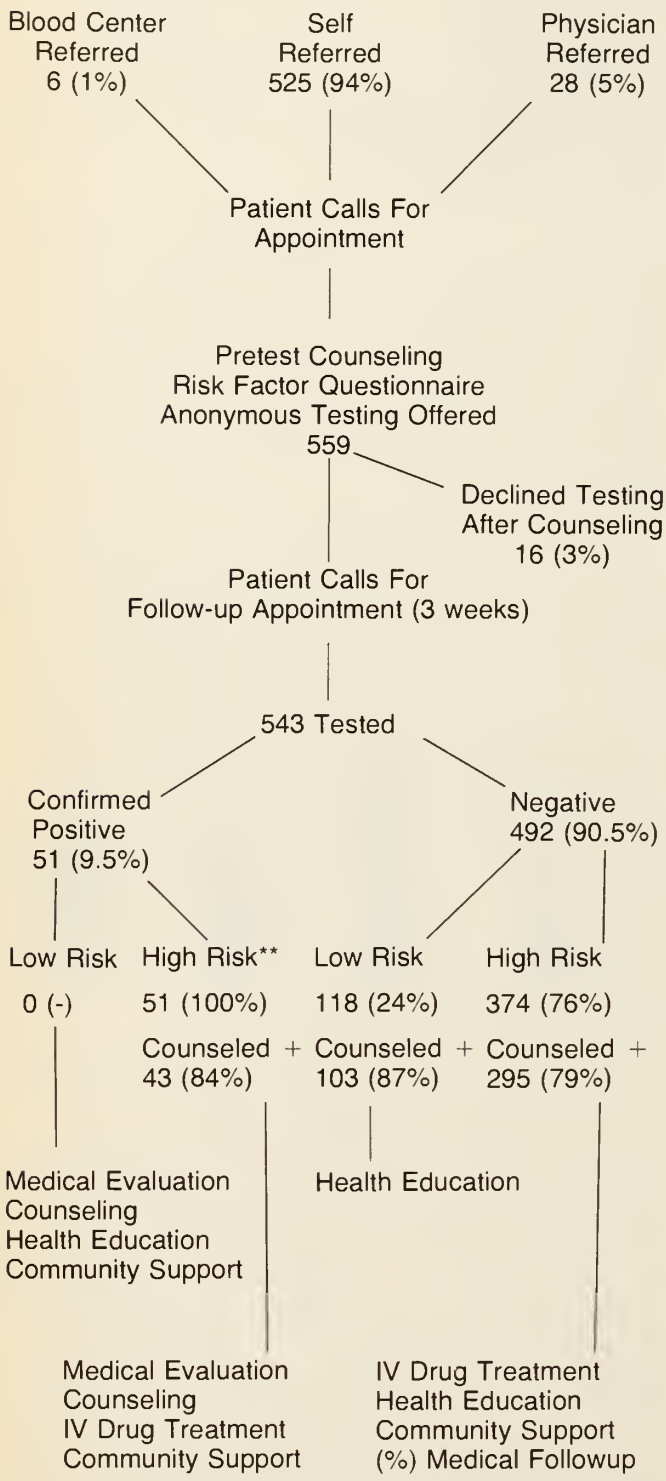
Because the specimens are submitted without personal identifying information, we are unaware of the circumstances and risk factors of positive-test persons at the time of testing. In order better to understand the epidemic, physicians of these patients will be asked for information about the risk factors of the patients and the epidemiological circumstances of the case at the time of reporting. The physician and patient will also be offered support, counseling, and referral services as necessary. All information is confidential and no information identifying the patient will be requested.

The Alternative Testing Site in the Rhode Island Department of Health

In June 1985 an "alternative testing site" (ATS) was established in the Department of Health with funds provided by the Centers for Disease Control. Since blood testing began, similar sites have been established throughout the country because of a general concern that persons from high-risk groups might donate blood in order to be tested for HIV infection.

The clinic has provided counseling and testing services for 2½ days per week and there is no charge. Clients are seen anonymously, and no identifying information is obtained. Appointments can be made by calling the AIDS activity program at the Health Department. During the first visit the client is given written information about AIDS and counseled about the test. Each client completes a questionnaire about his/her risk factors and reasons for attending the clinic and is then given a personal identification number.

Fig 2. Alternative Testing Counseling Site Activity, June 1985-August 1986 Rhode Island



**All risk groups.
+As of August 12, 1986

Table 2. Department of Health Alternative Testing Site Risk Factors of Test Site Attendees and Results of Screening for HIV/June 1985-August 1986

High Risk Groups (74.7%)	**N**	**Positives**	**(%)**
Gay/Bisexual Men	260	38	14.6
Intravenous Drug User	75	10	13.3
Both (Gay & IV Drug User)	4	1	25.0
Sex Partner of Bisexual	31	1	3.2
Sex Partner of IV Drug User	31	1	3.2
Sex Partner of Bisexual and IV Drug User	5	0	
Lower Risk Groups (25.2%)			
Previous Transfusion	21	0	
Prostitutes	1	0	
Sex With Prostitutes	25	0	
Sperm Donors	81	0	
	534	51	9.5

The patient must call to make an appointment for a follow-up visit, and the number must be presented in person in order to obtain the test result.

Between June 1985 and August 1986, 543 persons were counseled and tested at the clinic for HIV antibody. Ninety-four per cent of these were self-referred (Figure 2) and 75 per cent were from high-risk groups (Table 2).

It is noteworthy that over 50 per cent of those counseled said at the first interview that they would otherwise have donated blood in order to be tested.

Fifty-one (9.5 per cent) of those tested were positive for HIV antibody. Thirty-eight (75 per cent) of the positives were homosexual males (9 of whom were bisexual). They were drawn from a variety of occupational and socioeconomic backgrounds; 87 per cent were between 20 and 39 years of age. Two were currently serving in the armed forces. Eleven (30 per cent) were receiving health care, and 22 (5 per cent) were ill at the time of the first visit. Their symptoms included lymphadenopathy (9), weight loss (4), sore throat and respiratory symptoms (4), and anxiety and fatigue (4). Six (16 per cent) had a history of sexual exposure to a partner with AIDS or HIV infection, and two had sexual contact with an intravenous drug abuser. Fifteen (29 per cent) stated that they would otherwise have donated blood in order to obtain a test result.

Thirty-three of the 38 (87 per cent) have so far returned to receive their test results, but five failed to make an appointment and are lost to follow-up. At the second visit all were encouraged to seek medical evaluation and were referred to individuals and agencies in the region for counseling and support.

Ten persons (3 women and 7 men) who tested positive had a history of intravenous drug abuse, and 5 (50 per cent) had shared needles with persons known to have AIDS or HIV infection. Five were ill at the time of the first visit and two were receiving medical care. One had been previously diagnosed as having ARC while in prison. Three have not been seen again to be informed of their test results.

During its first year of operation the ATS has provided an important service by responding to the requests of over 500 persons, most of whom were from high-risk groups, for counseling and testing. The high prevalence of infection among clinic attendees and the low rate seen in the blood donor population suggests that the alternative testing site has diverted potentially contaminated blood away from the blood supply by counseling high-risk groups who may be infected.

In the future health education for prevention of infection among low- and high-risk groups in the community must be made widely available. But this should be augmented by opportunities for confidential testing and counseling of members of high-risk groups and their contacts in established health-care settings.

Anonymous testing has allowed high-risk groups to obtain testing in an atmosphere of concern about confidentiality, but it does not guarantee that infected persons obtain appropriate medical evaluation and follow-up. It is, therefore, essential that health care providers assume the responsibility for counseling and testing their patients in the course of their routine practices. Improved communication and cooperation between providers is necessary effectively to interrupt transmission of the infection.

The Rhode island AIDS and HIV Control Program

The Rhode Island Department of Health in conjunction with the Centers for Disease Control, the Association of State and Territorial Health Officers (ASTHO), and the Council of State & Territorial Epidemiologists has identified the following objectives for the public health response to the AIDS epidemic. 1) Surveillance for Disease; 2) Health Education for High- and Low-Risk Groups in the Population; 3) Professional Education; 4) Development of Programs to Prevent Transmission in High-Risk Situations; 5) Development of Networks with Professional and Community Groups; and 6) Creation of a State Interagency AIDS Task Force.

Objective 1: Surveillance and Epidemiological Studies

To study the prevalence and incidence of HIV infection and AIDS in the State through community surveillance and special studies of high-risk groups, in order to better define the magnitude of the problem.

Reporting: The syndrome of AIDS has been legally reportable in Rhode Island since 1983, but the AIDS control activity also maintains active surveillance for cases of AIDS-Related Complex (ARC) through contacts with health care providers. Asymptomatic infections identified by detection of antibodies to HIV using the ELISA test are not reportable at this time. All reports are held to be strictly confidential and are reportable to the Division of Disease Control of the Department of Health.

Confidentiality and the Law. Over the past three years surveillance for AIDS and HIV infection has been hampered somewhat by a general concern among high-risk groups about the confidentiality of test results. They fear that unauthorized disclosure of these may lead to ostracism at work, loss of jobs, loss of health insurance, and other forms of discrimination.

In 1978 Rhode Island enacted the Confidentiality of Health Care Act (5-37.3-1) which provides that a patient's confidential health care information shall not be released without the written consent of the patient. However, a ruling by the Rhode Island Supreme Court in January 1986 gave rise to some concern because it held that health-care information may be subject to subpoena by the courts. This prompted additional legislation passed in June 1986, which amended Chapter 9-17 of the General Laws titled "Witnesses." This provision states that health-care information and communications to health-care providers would be privileged information except when "(a) a patient raises his or her medical condition in a legal action; (b) when a court determines that the disclosure of health care information about a person is necessary to determine the perceptual capacity of that person as a witness in a legal proceeding and that the information is not available from any source other than a health care provider; (c) when a court order or the parties agree to a medical evaluation of a party or witness by a health care provider in order to facilitate the resolution of said legal action or (d) when the question of the competence of a decedent is at issue before the court."

The protection offered by this additional statute is appropriate, but has not yet been tested,

and the law may need to be strengthened further if the confidence and cooperation of high-risk groups is to be maintained.

Alternative Testing Sites: The Alternative Testing and Counseling Site in the Department of Health as been successful and will provide expanded services in the future. A full-time nurse counselor has recently been appointed to the AIDS activity. She will provide testing and counseling to clients and training for others providing testing services in the state. Because of the high percentage of AIDS cases associated with intravenous drug abuse in the state, an additional counseling/testing site is to be established that will provide services for this population. This site will be located at the Division of Substance Abuse at the State Medical Center in Cranston and will be operated jointly by the Department of Health and the State Division of Substance Abuse. It will provide counseling, medical examination, and support for all groups, but especially for intravenous drug abusers and their contacts.

Screening for Infection: The Department of Health does not advocate screening for evidence of infection in all persons in high-risk groups, but selective testing may be important (eg, for pregnant women in high-risk groups) and has a role in prevention of HIV transmission. Individual testing and counseling may reinforce general health education, but this should be used selectively and with the informed consent of the patient.

Testing may be very important for persons in low-risk groups who are heterosexual contacts of bisexual males or intravenous drug abusers and unaware of their exposure and subsequent risk of infection.

In all situations testing should be carried out only when confidentiality is assured and pre- and post-test counseling and support is available.

Contact Notification: Reaching out to persons who deny or are unaware of their risk is an important adjunct to general health education for behavior change. It is especially true for recalcitrant individuals who have not responded to other educational strategies. For those in low-risk groups it is important to contact these individuals in order to prevent further transmission of the virus and allow them to seek medical care and support. This "contact notification" should be conducted only in an atmosphere of complete confidentiality and with the informed consent of the infected person. Experienced staff of the AIDS activity who are familiar with interviewing techniques for sexually transmitted diseases are available to assist physicians and patients in referral of high-risk contacts for counseling and evaluation.

Objective 2: Health Education

To reduce HIV transmission through health education for risk reduction of high-risk groups and the low-risk general population of the state.

In the absence of a vaccine or effective treatment for HIV infection, behavior modification of high-risk groups through health education remains the principal tool available for interrupting transmission of the virus. It is also essential to educate low-risk groups and especially heterosexuals to dispel unwarranted fears and correct misunderstandings about the risks of infection. Homosexual and bisexual men are commonly a diverse and poorly defined group that is difficult to reach with conventional health-education approaches. They vary in their knowledge about AIDS and commitment to change in sexual practices, and it will be necessary to use several complementary strategies to reach those at highest risk. To achieve this the AIDS health education activity of the Department of Health will be working with other agencies, staff of sexually transmitted disease clinics, and community groups to evaluate the needs for health education in this population and to implement education programs to reduce transmission.

Intravenous Drug Abusers: It has been estimated that there are approximately 1,000 intravenous drug abusers receiving medical care in the state and about 5,000 other addicts who are receiving none (personal communication, R. Freeman). The single methadone maintenance program in the state has at present approximately 200 clients under treatment and a long waiting list. These and other services should be made more available if attempts to stop transmission by changing needle-sharing behavior are to have a chance of success.

The needle-sharing behavior of intravenous drug abusers poses the greatest challenge for achieving change through health education. Several intervention strategies have been proposed to reduce transmission of AIDS in this group. They include distribution of clean needles and needle exchange, and education to encourage cleaning and sterilizing of shared needles. These have been controversial and when tried have met with variable success. Similar measures may have a role in control programs in Rhode Island, but must be evaluated carefully.

The State Department of Mental Health, Re-

tardation and Hospitals (MHRH), Division of Substance Abuse, is currently funding 20 programs that provide services in settings where health education can be provided for substance abusers. Education programs for staff and clients are being developed to implement in these settings.

High-Risk Women: Several agencies currently provide services for high-risk women who may become infected and transmit the AIDS virus.

The Division of Family Health in the Department of Health provides funds for family planning programs and prenatal care in hospitals and clinics throughout the state. Many of these provide services for sexually active and pregnant adolescents, intravenous drug abusers, and prostitutes.

The Department for Children and Their Families provides services for over 4,000 adolescents, of whom approximately 1,000 are individuals between 14 and 18 years of age who are at increased risk.

Staff of these agencies will be cooperating with the AIDS program of the Department of Health to evaluate the educational needs of these groups and devise intervention programs for counseling and risk reduction.

Public Education: Education of the general public, and especially sexually active adolescents, is urgently needed to inform them about the transmissibility of the virus and emphasize the risk of heterosexual spread of the infection.

Thus far the media have had a prominent role in informing the public about AIDS and about the epidemiology of HIV infection.

Now more focused education must be provided by health professionals through the written and broadcast media by public presentations, and educational programs in schools and work places.

The AIDS control activity will be working with the Division of Health Promotion in the Department of Health to develop educational programs following community surveys to assess the levels of public knowledge about AIDS.

The Wellness Wagon, an established mobile consumer health survey unit based in the Division of Health Promotion, will be used to study the levels of knowledge in school students (14 to 18 years of age) in cooperation with local school departments. Community studies are also planned using a random digit dialing telephone survey. Education initiatives will be developed and implemented based on the results of these and other surveys nationwide.

In April of 1986 the Department of Health was awarded funds for a cooperative agreement with the Centers for Disease Control to expand health education and risk-reduction activities and carry out the programs mentioned above. A health educator and a disease control representative were recently appointed to the Division of Disease Control to coordinate these activities.

Objective 3: Professional Education

To provide continuing education to health professionals that will enable them to provide counseling, medical evaluation, and support to infected persons and those in high-risk groups.

Over the past two years the Rhode Island Department of Health has been actively involved in educating health-care professionals about AIDS through lectures, seminars, and published documents.

Several occupational groups (fire fighters, correctional officers, health and rescue workers, morticians, and educators) have expressed concerns about potential exposure to the virus in their work. In response to this, several guidelines have been developed which are available from the Rhode Island Department of Health. These will be updated as necessary.

Objective 4: Special Programs

To provide special programs for persons in high-risk environments.

In certain unique situations there may be a need to develop educational programs and special policies for prevention of HIV transmission. This may be appropriate in institutions such as schools for the mentally handicapped, shelters "for the homeless," dialysis units, and other health care settings.

Programs and policies may also have to be developed to provide for individuals in high-risk groups who are unresponsive to health education measures and may disseminate the virus in the community.

The AIDS control activity has issued guidelines for prevention of HIV transmission in several of these settings and will continue to do so for other situations as the need arises.

Objective 5: Development of Community Networks

The needs of person infected with HIV and those with AIDS are varied and complex. They require services that range from counseling and support to intensive hospital care.

The impact of AIDS has been felt widely in a number of public and private agencies through-

out the state. Several community groups have become active in AIDS prevention. These include Rhode Island Project AIDS (RIPAIDS), the Rhode Island Alliance for Gay & Lesbian Civil Rights, Dignity, Network, church groups and others. They have acted as advocates for persons with AIDS, provided services for those who need help, and have mobilized to educate high-risk groups.

The contributions of these groups are important and need to be integrated. It is now more important than ever to develop networks involving state agencies, health care providers and community groups to interrupt the transmission of HIV in the community and to ensure appropriate care for those infected with HIV.

Objective 6: Interagency Task Force

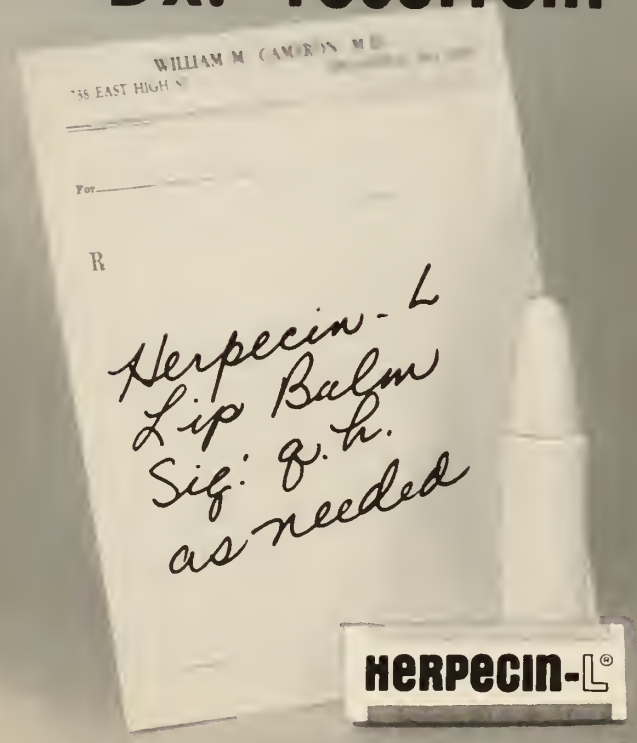
An advisory committee was established in August 1983 to assist the Rhode Island Department of Health in developing strategies for the control of the AIDS epidemic. The membership includes health-care providers, members of state agencies, and representatives of community groups concerned about AIDS.

Over the last three years the committee has provided invaluable support, but there is now a need for an expanded body that will consider a variety of issues and develop authoritative guidelines within a framework of a state plan for AIDS control.

The advisory committee will soon be reconvened to form a task force that will include representatives from state agencies, the governor's office, health-care providers, and representatives of community organizations to address these goals.

AIDS and HIV infection are likely to become a much greater problem in Rhode Island in the future. Since a breakthrough in treatment with vaccines or drugs seems remote at present, control measures through health education must continue. Control of AIDS in the community must be based upon accurate knowledge of the risk of disease obtained through surveillance and special studies, and altering behavior through health education. Conservative sexual practices and control of intravenous drug abuse should be promoted through targeted education in media campaigns to high-risk groups. Health-care providers also need regular updated information. Vigorous implementation of these measures can stem the tide, but it seems unlikely that they will stop transmission.

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms . . .** blisters **never formed . . .** remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L . .** proven **far superior.**" DDS, PA

"All patients claimed **shorter duration . . .** at **prodromal symptoms . . .** HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

SEMI-ANNUAL CALENDAR OF CONTINUING MEDICAL EDUCATION EVENTS

NOTE: Lectures and courses are listed by the date, sponsor, topic, speaker, and telephone number for additional information. Please call the contact number for specific information about the program.

FEBRUARY

6 Institute of Mental Health, Psychiatric Case Conference, Aimee Schwartz, MD, Walter Brown, MD (Moderator), 464-2458

11 Emma Pendleton Bradley Hospital, Pediatric Seminar Series — "Children Who Need Referral," Martin Irwin, MD, Sponsor — The Division of Child & Adolescent Psychiatry, Brown University Program in Medicine, 434-3400, ext. 318

20 Institute of Mental Health, Psychiatric Case Conference, Ronald Stewart, MD, Walter Brown, MD (Moderator), 464-2458

23 The Woonsocket Hospital, "Treatment of Diabetes in the Elderly," Stephen Gambert, MD, Sponsor — ROERIG, 767-3211, ext. 2310 or 2311

27 Institute of Mental Health, IMH Forum — "Treatment Philosophy of the Forensic Unit of the Institute of Mental Health, Ronald Stewart, MD, 464-2458

MARCH

6 Institute of Mental Health, Psychiatric Case Conference, Sidney Heisler, MD, Walter Brown, MD (Moderator), 464-2458

6 The Memorial Hospital, Kenney Day Program — Seminar — Special Annual Event, Sponsor — The Memorial Hospital & various pharmaceutical companies, 722-6000, ext. 2142

7 Brown University Program in Medicine, "Emotional Aspects of Cardiovascular Disease," Speaker to be announced, 863-1139

11 Emma Pendleton Bradley Hospital, Pediatric Seminar Series — "Sleep Disorders in Infants and Children," Thomas F. Anders, MD, Sponsor — The Division of Child & Adolescent Psychiatry, Brown University Program in Medicine, 434-3400, ext. 318

16 The Woonsocket Hospital, "Practical Management of Low Back Pain," Charles Barbara, MD, Sponsor — Merck, Sharp, & Dohme, 767-3211, ext. 2310 or 2311

20 Institute of Mental Health, Psychiatric Case Conference, Sarah R. Zamari, MD, Walter Brown, MD (Moderator), 464-2458

27 Institute of Mental Health, IMH Forum — "Behavior Sciences and Administrative Psychiatry," John Karkalas, MD, 464-2458

APRIL

3 Institute of Mental Health, Psychiatric Case Conference, Max Faintych, MD, Walter Brown, MD (Moderator), 464-2458

4 Women and Infants Hospital of RI, Annual Anesthesia Symposium, Speaker(s) to be announced, 274-1100, ext. 1565

8 Emma Pendleton Bradley Hospital, Pediatric Seminar Series — "Failure to Thrive and Parenting," Charles A. Malone, MD, Sponsor — The Division of Child and Adolescent Psychiatry, Brown University Program in Medicine, 434-3400, ext. 318

17 Institute of Mental Health, Psychiatric Case Conference, John Melchiona, MD, Walter Brown, MD (Moderator), 464-2458

20 The Woonsocket Hospital, "Use of Calcium Channel Blockers in Treating Hypertension," Sponsor — Roche, 767-3211, ext. 2310 or 2311

24 Institute of Mental Health, IMH Forum — "Psychosocial Rehabilitation Program at The Institute of Mental Health," Hugo Halo, MD, Geronimo Torres, MD, John Karkalas, MD, 464-2458

MAY

1 Institute of Mental Health, Psychiatric Case Conference, Saul Martin, MD, Walter Brown, MD (Moderator), 464-2458

15 Institute of Mental Health, Psychiatric Case Conference, Christopher Joo, MD, Walter Brown, MD (Moderator), 464-2458

18 The Woonsocket Hospital, "Current Antiviral Therapies," Nelson M. Gantz, MD, Sponsor — Burroughs Wellcome Co., 767-3211, ext. 2310 or 2311

21 Brown University Program in Medicine, "Diabetes Update: Newport '87," Aaron Vinik, MD, Ronald Klein, MD, Julio Santiago, MD, John E. Gerich, MD, Sponsor — RI Affiliate — American Diabetes Association, 863-1139

29 Institute of Mental Health, Psychiatric Case Conference, Hugo Halo, MD, Walter Brown, MD (Moderator), 464-2458

JUNE

12 Institute of Mental Health, Psychiatric Case Conference, Frank Jones, MD, Walter Brown, MD, (Moderator), 464-2458

15 The Woonsocket Hospital, "Cardiac Imaging," Michael Bettman, MD, Sponsor — Ayerst, 767-3211, ext. 2310 or 2311

26 Institute of Mental Health, Psychiatric Case Conference, Sarah Zamari, MD, Walter Brown, MD (Moderator), 464-2458

26-28 Brown University Program in Medicine, "Locking Nail/External Fixation Course," Speaker(s) to be announced, 863-1139

JULY

10 Institute of Mental Health, Psychiatric Case Conference, Constantine Loures, MD, Walter Brown, MD (Moderator), 464-2458

24 Institute of Mental Health, Psychiatric Case Conference, Sidney Heisler, MD, Walter Brown, MD (Moderator), 464-2458

CONTINUING SERIES

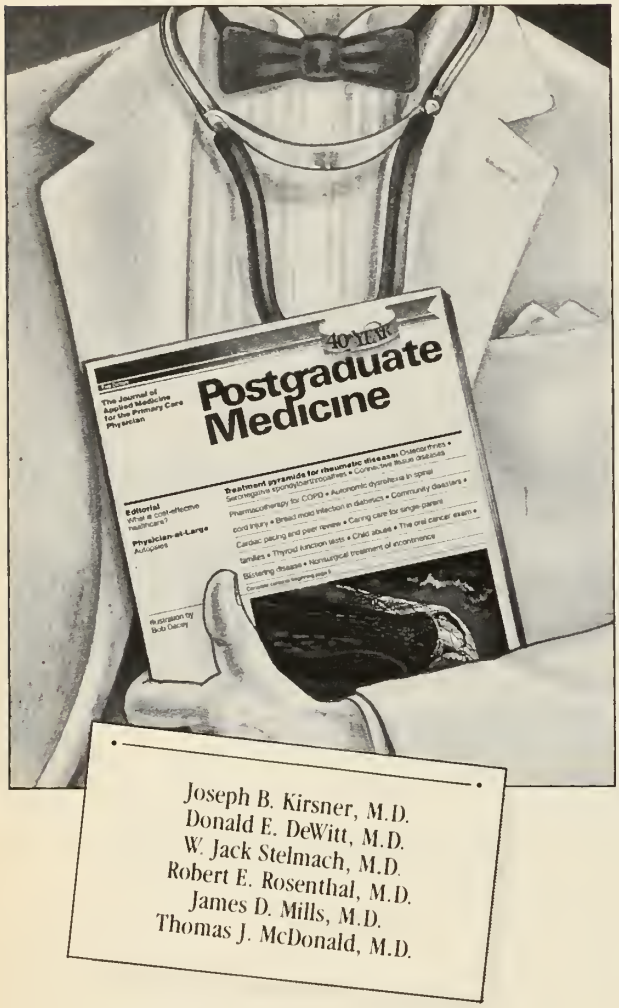
The Memorial Hospital (722-6000, ext. 2142)

Monday	12:15 pm	Medicine/Family Medicine — Core Curriculum Conference on Current Clinical Topics
Tuesday	8:30 am	Cardiology Conference — Challenging Cardiologic Concepts
Monday, Tuesday, Thursday & Friday	10:15 am	Radiology Conference
Tuesday (except last Tues. of month)	8:00 am	Hematology/Oncology Conference
Last Tuesday of each month	7:30 am	Tumor Board Conference
Wednesday	8:00 am	Pediatric Grand Rounds
Wednesday	10:00 am	Medical Grand Rounds
Wednesday	3:00 pm	Pathology Conference
Alternating Wednesdays	12:15 pm	Pulmonary Case Review
Alternating Wednesdays	12:15 pm	Infectious Diseases Conference
Thursday	12:15 pm	Family Practice Grand Rounds
Thursday	8:00 am	Surgical Grand Rounds
Thursday	8:00 am	Orthopedic Conference
Thursday	8:00 am	OB/GYN Conference
Thursday	4:30 pm	Surgical Service Conference

Woman & Infants Hospital

Tuesday	7:30 am	Tumor Board Meeting (274-1100, ext. 1588)
Wednesday	7:45 am	Perinatal Management Conference (274-1100, ext. 1229)
Saturday	8:00 am	Grand Rounds (274-1100, ext. 1584)
Saturday	9:00 am	Ob-Gyn Lecture (274-1100, ext. 1584)

FAMOUS PHYSICIANS ARE SHOWING UP FOR OUR 40th YEAR CELEBRATION.



Joseph B. Kirsner, M.D.
Donald E. DeWitt, M.D.
W. Jack Stelmach, M.D.
Robert E. Rosenthal, M.D.
James D. Mills, M.D.
Thomas J. McDonald, M.D.

Read Every Issue From Cover to Cover:

January
Symposium: Biliary Tract Disease
Special Article: Gastroenterology 1947-1987 . . . . Joseph B. Kirsner, M.D.

February 1
Symposium: Focus on Family Practice . . . . Donald E. DeWitt, M.D. coordinator
Special Article: Family Practice 1947-1987 . . . . W. Jack Stelmach, M.D.

February 15
Symposium: Emergency Medicine . . . . Robert E. Rosenthal, M.D. coordinator
Special Article: Emergency Medicine 1947-1987 . . . James D. Mills, M.D.

March
Symposium: Otolaryngology in Primary Care . . . . Thomas J. McDonald, M.D. coordinator
Special Article: Otolaryngology 1947-1987 . . . . Thomas J. McDonald, M.D.

40 YEAR
Postgraduate Medicine

Every Issue is a Celebration of Clinical Information

FOR SALE: BEST OFFER

BIO DYNAMICS AUTOMATIC CELLTRACK 5

BIO DYNAMICS UNIMETER 300 K 18 CHEMISTRIES INCLUDING K

433-4300

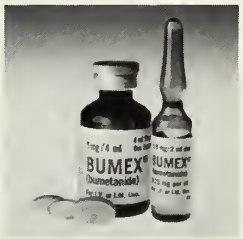
PRIME OFFICE SPACE AVAILABLE

Adjacent To
Kent County Hospital
Will finish to your specifications
401-732-0406

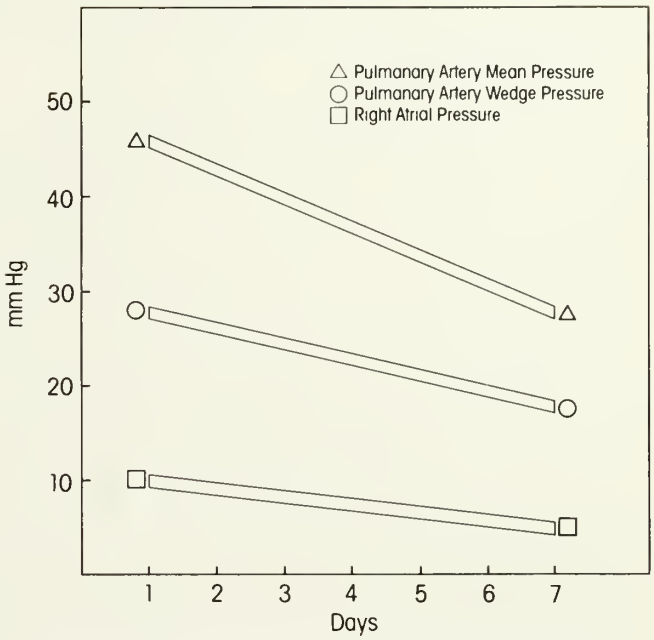
Bumex®
bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml
and 10-ml vials (0.25 mg/ml)

REDUCES FLUID OVERLOAD and eases the burden on the failing heart



Significantly improves hemodynamics



Ten patients with CHF showed marked hemodynamic improvement after seven days of BUMEX® (bumetanide/Roche) (mean values ± SE) Adapted from Olesen, *et al* [1]

References: **1.** Olesen KH, *et al Postgrad Med J 51*(Suppl 6) 54-63, 1975 **2.** Handler B, Dhingra RC, Rasen KM *J Clin Pharmacol 21* 706-711, Nov-Dec 1981 **3.** Brater DC, *et al Clin Pharmacol Ther 34* 207-213, Aug 1983 **4.** Brater DC, Fox WR, Chennavasin P *J Clin Pharmacol 21* 599-603, Nov-Dec 1981 **5.** Davies DL, *et al Clin Pharmacol Ther 15* 141-155, Feb 1974

BUMEX®
bumetanide/Roche
0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)

BUMEX® (bumetanide/Roche)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome
Almost equal diuretic response occurs after oral and parenteral administration of Bumex If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity
CONTRAINDICATIONS: Anuria Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment
WARNINGS: Dose should be adjusted to patient's needs Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risks to the patients
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved The potential for ototoxicity increases with intravenous therapy, especially at high doses
Patients allergic to sulfonamides may show hypersensitivity to Bumex
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets Hyperuricemia may occur Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency Bumex may increase urinary calcium excretion
Possibility of effect on glucose metabolism exists Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics.
Probenecid should not be administered concurrently with Bumex
Concurrent therapy with indomethacin not recommended
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage
Interaction studies in humans have shown no effect on digoxin blood levels
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
Bumetanide may be excreted in breast milk
Pediatric Use: Safety and effectiveness below age 18 not established.
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease)
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection.
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts Increases in urinary glucose and urinary protein have also been seen
DOSAGE AND ADMINISTRATION:
Oral Administration The usual total daily dosage is 0 5 to 2 0 mg and in most patients is given as a single dose
Parenteral Administration: Administer to patients (IV or IM) with GI absorption problem or who cannot take oral The usual initial dose is 0 5 to 1 mg given over 1 to 2 minutes If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day
HOW SUPPLIED: *Tablets,* 0 5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescription Paks of 30, Tel-E-Dose® cartons of 100 Imprint on tablets 0 5 mg—ROCHE BUMEX 0 5, 1 mg—ROCHE BUMEX 1, 2 mg—ROCHE BUMEX 2
Ampuls, 2 ml, 0 25 mg/ml, boxes of ten
Vials, 2 ml, 4 ml and 10 ml, 0 25 mg/ml, boxes of ten

ROCHE®
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc
Nutley, New Jersey 07110

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

OVERLOAD

Reduce fluid volume and improve hemodynamics in CHF

Edema due to congestive heart failure often demands highly effective diuresis to reduce the fluid load on the failing heart. Bumex® (bumetanide/Roche) is the next generation in loop diuretic therapy for three powerful reasons. It moves out an unsurpassed volume of fluid and sodium, resulting in significant reductions in edema and right atrial and pulmonary artery wedge pressures.[1,2] It's almost completely absorbed through the GI tract, so it's easy to titrate.[3] And Bumex completes high-volume diuresis fast—within four hours at usual doses.[4,5] Your patients spend less time in diuresis, more time in normal activities.

Bumex has a good safety profile; however, as with all loop diuretics, Bumex, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion, including hypokalemia. Serum electrolytes should be monitored periodically, especially in patients on low salt diets or those treated for prolonged periods or on high doses.

Bumex®
bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets, 2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

First line loop diuretic therapy

Please see references and summary of product information on preceding page.

Copyright ©1986 by Hoffmann-La Roche Inc. All rights reserved.

Rhode Island Medical Journal

February 1987
Volume 70, Number 2

How are Cambodians Adapting To Western Medicine?
See page 73

CONTRIBUTIONS

65 The World of Hunger

73 Traditional Cambodian Health Beliefs and Practices

79 Health Care 1986-87

59 EDITORIAL

61 SPECIAL REPORT
An HMO Experience

63 Commentary

69 Information for Authors

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:

- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE

OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

Propranolol is not significantly dialyzable.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely; or INDERAL should be discontinued (gradually if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal. nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. bronchospasm.

Hematologic. agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985;145:1321-1323.

6412/187

Ayerst® AYERST LABORATORIES
New York, NY 10017

© 1986 Ayerst Laboratories

ZOVIRAX®
(acyclovir)
CAPSULES

Prevent genital herpes recurrences month after month with daily therapy.

(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

Please see last page of this advertisement for brief summary of prescribing information.

ZOVIRAX®
(acyclovir)
CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes, as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next page.

Prevent recurrences month after month*

ZOVIRAX®

(acyclovir)

CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psychosocial difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies,. the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤10 ml/min/1.73/m².

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200"- Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

---

*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

Wellcome | Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Copr. © 1986 Burroughs Wellcome Co. All rights reserved. 86-ZOV-5

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℠

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

Rhode Island Medical Journal

February 1987
Volume 70, Number 2

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA MAY 21 1987

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Jack A. Perkins
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Guy A. Settipane, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

***Edward R. Feller, MD**

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Peter D. T. Clarisse, MD
President

Richard G. Bertini, MD
President-Elect

Milton W. Hamolsky, MD
Secretary

Kenneth E. Liffmann, MD
Treasurer

Herbert Rakatansky, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

John J. Coughlin, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401 331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

Dr. Osborne just lost his patients.
All of them.

The simple fact is, Dr. Osborne's billing service just went out of business. And that leaves Dr. Osborne with a fairly complex problem: The business failure of a billing service can cost a physician *up to a quarter of a year's income* due to unbilled services, uncollected receivables, and lost records.

The mistake that our hypothetical Dr. Osborne made is no myth. In reality, many physicians believe there are no significant differences between billing services. Different software packages, perhaps. Price. But beyond that, a billing service . . . is a billing service.

The truth is, it makes a *big* difference who handles your practice billing. Things can and do go wrong—like misbilling and mismanaged or even unprofessional collection procedures. These and other problems not only cost a practice financially, but can impact on patient satisfaction and goodwill, which is perhaps most costly of all.

If you really don't want to worry about billing, take a close look at how you do your billing now. And then call us. We'll be pleased to demonstrate our stability and track record. To explain our billing and collection procedures and our patient relations standards. And to show you how our customized services can meet your practice needs and improve your cash flow.

Call us soon. Because you have everything to lose.

pms
Professional
Management
Services, Inc.

(401) 521-6310

Boston
W. Springfield, MA
Philadelphia
Providence
Hartford

TABLE OF CONTENTS

59 **EDITORIAL**
A New Type of Hospital Consortium

61 **SPECIAL REPORT**
An HMO Experience
Jeffrey Austerlitz, MD

63 **Commentary**
Charles M. Cutler, MD

CONTRIBUTIONS

65 **The World of Hunger**
Program of Brown University to Address World Hunger Problems of the Present and Future
Robert W. Kates, PhD

73 **Traditional Cambodian Health Beliefs and Practices**
Understanding Cambodian Traditions Will Facilitate Their Care In a Western Setting
Louise Aronson, BA

79 **Health Care 1986-87**
"It Was the Best of Times, It Was the Worst of Times"
H. Denman Scott, MD

COVER: *Picture provided by Cambodian Society of Rhode Island*

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml (*1 teaspoonful*) contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg (*warning: may be habit forming*); alcohol, 3.5 percent; in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

EDITORIAL

A New Type of Hospital Consortium

In recent years several hospitals in Boston and elsewhere have perfected agreements with pharmaceutical manufacturers whereby research at the hospitals is supported financially by the corporations and the latter in turn have access to the results of the investigations. This kind of symbiosis, although still relatively new, appears to be working out to the advantage of both.

Recently Brigham and Women's Hospital, the Harvard affiliated institution in Boston, announced a new kind of consortium. The Hospital Corporation of America, the largest for-profit hospital chain in the country, and the Brigham have consummated an unusual agreement by which they will share the hospital's expertise and the company's purchasing power.

The three-year arrangement provides that the Brigham will work with the Nashville-based corporation to develop continuing medical education courses for use in the 470 hospitals of the corporation scattered around the world. It will also assess the quality of patient care in the 18 New England hospitals which are owned or managed by the corporation. The corporation will finance these services and in turn will grant to the Brigham use of the corporation's efficient purchasing system.

The corporation has links with several teaching hospitals, including management contracts with some, but the new arrangement differs from any of these. It certainly differs from the attempt to buy the McLean psychiatric hospital from the Massachusetts General Hospital, which transaction was blocked by vigorous opposition from the academic medical staff.

The new arrangement makes available to Brigham the management skills of the corporation, while leaving undisturbed care of the poor, education of health professionals, and research. At the same time it will provide the hospital with the purchasing clout of the corporation, especially in large items. It will be interesting to watch this experiment.

Seebert J. Goldowsky, M.D.

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

We've become the largest full service medical lab in Rhode Island...*because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011

CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry Narragansett • West Warwick • Cumberland

SPECIAL REPORT

HMO Medicine: A Personal Experience

When I returned recently to Rhode Island and heard of the changes the medical system here was going through, I felt it important to write this paper to record my impressions.

I first thought about joining an HMO when I was in my residency. It seemed a comfortable, uncomplicated place to practice medicine without all the risks of private practice. I was not a business manager and had no interest in losing patient-care time worrying about my charges, buying equipment, or hiring and firing staff. I also like the idea of a guaranteed income. In any case, before going out into the real world, I had a four-year commitment to the Public Health Service. This experience solidified my commitment to HMOs.

As chief of medicine in a small Indian Health Service hospital in Oklahoma during the time of Reaganomics, I learned what cost-effective medicine was and became quite good at it. People were always looking over my shoulder at my testing pattern, and I had to be ready to defend any test I ordered. With limited in-house resources, all but the simplest tests were referred elsewhere. Such complicated procedures as echocardiograms, mammograms, and nuclear medicine were referred, not to mention things such as coronary angiography and bypass surgery or CT scanning. Any test done outside our facility was scrutinized closely, and often, because we had arleady spent all of our allocated monies, was to be paid for by the patients. You can imagine that few of the patients coming to a public facility could afford extensive testing. The tests often went undone, and I was forced to manage these patients anyway. I was very surprised at how well close clinical evaluation allowed me to manage my patients without extensive laboratory support. Not only did this help me reduce the number of tests I thought I needed, but it also made me realize that when I did want a test or an operation for one of my patients, I wanted to be sure it was done and not have it delayed because the patient could not afford it. The HMO, because of guaranteed first dollar coverage, provided this assurance. When my commitment with the Public Health Service was coming to an end, I decided the HMO was the way for me to go. I knew that HMOs try to control the lives of their doctors to a certain extent, but after all I had survived four years in the government system. How could anything be more controlling?

In choosing an HMO, I was very careful to pick one which promised noninterference with admissions and testing. I was also promised continuity of care for my patients. My patients would feel an allegiance to me as I would to them. When they became ill, they would see me and return appointments would be routine.

In early July, I entered into my new position as a staff internist for a large HMO, which several years earlier had been bought by a large national for-profit corporation. This HMO was in a strong financial position and was expanding rapidly. Shortly thereafter, I inherited the patients of the medical director, who had become a full-time administrator. These patients were long-term patients of the system, many with complicated medical problems. Also, because I was the new kid on the block with the most open appointment

slots, I began getting the new patients as well as any patients with acute medical problems. I very quickly came to see that most patients did not identify with any physician and that the system did not identify patients with any physician. A patient calling in for an appointment was given the next available appointment without regard to the primary physician.

As a for-profit corporation which depended for its survival on seeing as many patients as possible, giving as little service as possible, the perception was that the patients wanted most to be able to see a physician — any physician — whenever they wanted or had a problem. Because of this 50 per cent of all appointment slots were kept open for same-day appointments. These slots were sancrosanct, and follow-up visits were less important. A patient for follow-up may have to wait several months to be seen, while a new patient or a patient with a cold got immediate service. The schedule followed a modified wave format to allow for the number of no-shows that were thought to occur routinely. This schedule was the same for all physicians, internists to family practitioners and pediatricians. The schedule also did not differentiate between the needs of a 19-year-old with a jammed finger and those of a 70-year-old with multiple problems just transferring into the system for his care. The HMO physician was expected to refill the medications until he could fully evaluate the patient over the course of the next several visits. Of course, as I have already indicated, follow-up visits often took months and full physicals took even longer.

Because of the scheduling system, which was totally out of the physician's control, it was not uncommon for me to see 25-30 patients a day on top of my hospital load. I was always running one-two hours late with patients having to wait as long as three-four hours at times. Visits scheduled late in the day were often rushed because of the lateness of the hour.

An additional pressure was to save on emergency room visits by seeing patients in the office, often trusting the opinion of the triage nurse in the ER as to whether or not the patient was stable enough to be transported to the clinic. It was not felt to be cost-effective to have our own emergency room or acute care center, because that would entail hiring more personnel. There was also a subtle pressure to handle problems with which any individual physician might not feel comfortable. For me, this meant suturing lacerations.

Of interest is the fact that the local branch of the HMO was one of two branches that earned a profit for this corporation. It was not because of cost containment or efficiencies, but because it was operating with a physician shortage. While purportedly not intentional, but a result of the rapid growth and time lag in hiring qualified physicians, this shortage had existed for the entire eight-year history of the HMO. Any mention of hiring interim physicians to relieve some of the load was scoffed at as inappropriate as the current level of care was deemed appropriate. Also, any attempt to individualize the schedule to meet the needs of any individual — patient or physician — was denied. Because of all of these factors, there was a tremendous physician turnover with many of my patients having seen three or four physicians in the system for continued medical care in the last year.

Of particular interest was the medical director, himself an internist who left private practice to be half-time clinician and half-time medical director. During our early discussions, his interests in quality care, continuity of care, and preventive medicine seemed to parallel mine. However, in our later discussions, he was quite frank in saying that our first allegiance must be to the corporation, as long as quality was not affected.

Unfortunately, his concept of quality was very evident in examining the charts of patients he had been following. Many of those with chronic diseases such as hypertension and diabetes had not been examined for upwards of eighteen months despite multiple visits. Many patients also had never had their medications re-evaluated since joining the HMO. This was what was considered to be quality medicine in this HMO. Furthermore, physician assistants were utilized as independent practitioners, with physicians being asked to co-sign stacks of charts at the end of the day without having supervised the handling of the cases.

HMO patients often do not expect top quality care when they join, believing that first-dollar coverage will make up for this reduction in quality. I heard this many times during my association with the HMO, both from dissatisfied patients and from colleagues in other HMOs.

To me, this added up to poor quality medicine, a type of medicine I was unwilling to practice. After four months of actively and vociferously attempting to change the system and a month of trying at least to suit my own personal needs, I could take it no longer and submitted my resignation. I realized that the only way to control

my own destiny and to practice high quality medicine was to enter private practice.

While not inherently bad, HMOs, especially staff models because of their size, must discourage flexibility and individuality. Therefore, quality must be reduced to the lowest common denominator — financial constraints, the quality of the medical director, or the expectations of the patients, which often adds up to inferior quality.

If this is the future of American medicine, I fear our patients are in for medicine of quite a different sort than they have come to expect. We too are in for quite a change, and for many of us, it is not a welcome one. □

Jeffrey Austerlitz, M.D.

Upon our invitation to comment on Dr. Jeffrey Austerlitz's view of Health Maintenance Organizations, Dr. Charles M. Cutler sent us this reply.

Doctor Austerlitz's comments and experiences in an HMO before coming to Rhode Island are very disquieting, and fortunately are not representative of staff or group model HMOs generally. His paper presents a specific case report that describes the symptoms of a disease which can affect fee-for-service practice as well as prepaid practice — the lack of a commitment to excellence and quality in health care.

The commitment to quality health care is important at Rhode Island Group Health Association (RIGHA) from both a professional and business standpoint. Consumers may be willing to sacrifice quality for cost when purchasing some goods and services. However, I doubt that this is the case for health care. If consumers perceived HMOs as cutting back on or providing poor quality care, the plans would have no members. From a purely business standpoint, therefore, it makes good sense to assure high quality health care to be able to attract and retain members. This goal seems to have been achieved in most plans: A Louis Harris Poll[1,2] of HMO members shows that most feel access to physicians (76 per cent), preventive services (84 per cent), waiting time for appointments (73 per cent), waiting times in the office to see the physician (78 per cent), helpfulness of physicians and staff (76 per cent), and quality of physician (75 per cent) are equal to or better through HMOs than fee-for-service in the community in general.

HMOs are successful when they maintain their members' health, not when members are ill. This is one of the reasons why routine screening, follow-up visits, and health education are covered by many HMOs. It therefore makes sense for the doctor practicing in an HMO to re-evaluate patients periodically and to encourage patients to undergo screening when indicated. Supporting this is comparison of the number of visits made by patients with rheumatoid arthritis which showed no difference between patients treated by HMOs and fee-for-service practice. Earlier studies by the General Accounting Office (GAO)[3] showed HMO members see physicians more than those in other insurance plans.

Quality is carefully controlled by federally qualified HMOs which are required to have active quality assurance programs. These programs address issues of accessability, availability, and outcomes of care provided to the HMOs patients. They insure that patients are afforded high quality care as well as assure that physicians are providing the necessary services to members. This mechanism for evaluating quality in prepaid practices is not matched by a similar review mechanism in fee-for-service practice. A study reviewing quality of care showed that of 80 valid measurements HMOs were superior to fee-for-service practices in 53, equal in 19, and not as good in 8.[4]

The professional reputation of individual physicians in the practice is the collective reputation

of the group. RIGHA has been able to attract and retain excellent physicians because of the organization's commitment to quality health care. While there are inherent demands to be productive and cost effective, this is not at the expense of the quality of care provided to our patients. Clearly the physician's responsibility is to be the patient's advocate. The question faced by HMO physicians is not whether to provide services, but to find the most cost beneficial method of providing those services. Our ability to recruit high quality physicians who are frequently sought after as instructors in the teaching hospitals and Brown University Program in Medicine speaks to this point. The very low turnover rate of physicians at RIGHA shows that HMOs can provide a satisfying practice for physicians. This is supported nationally by a recent study of primary care and specialty physicians which suggests a high degree of satisfaction with group practice.[5]

Finally, the success or failure of an HMO will be dependent on its ability to provide high quality service to members, to attract and retain qualified and satisfied physicians, and to offer competitive premiums. We feel our Staff Model HMO has met this challenge and will continue to do so in the future.

Charles M. Cutler, MD
Medical Director of RIGHA

References

1 Louis Harris and Associates, Inc. American Attitudes Toward Health Maintenance Organizations 1980.

2 Louis Harris and Associates, Inc. A Report Card on HMO's 1980-1984.

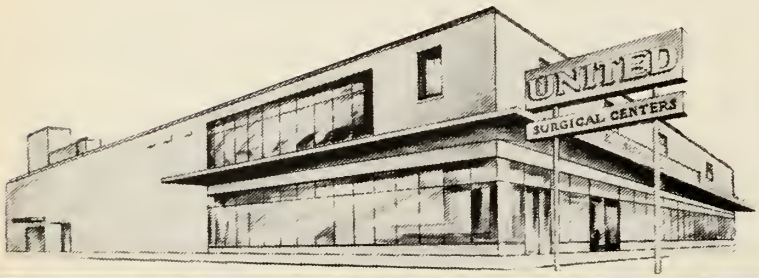
3 Edward H. Yelin, Ph.D., Curtis J. Henke, Ph.D., Jane S. Kramer, M.Sc., Michael C. Nevitt, Ph.D., Martin Shearn, M.D., and Wallace V. Epstein, M.D. Comparison of the Rheumatoid Arthritis in Health Maintenance Organizations and Fee-For-Service Practices. The New England Journal of Medicine, April 1985; Vol. 312, Pgs. 962-967.

4 Frances C. Cunningham and John W. Williamson, MD. How Does the Quality of Health Care in HMO's Compare to That in Other Settings? An Analytic Literature Review: 1958 to 1979. The Group Health Journal, Winter 1980. Pg. 4.

5 Derick P. Pastemak, Waneta C. Tuttle, and Howard L. Smith. Physician Satisfaction in Group Practice: A Comparison of Primary Care Physician With Specialists. GHAA Journal Spring 1986; Vol. 7, Pgs. 50-60.

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS
The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

The World of Hunger

Program of Brown University to Address World Hunger Problems of the Present and Future

Robert W. Kates, PhD

The world of hunger is the everyday world of up to a billion of the world's people. It is a world where there is not enough food; or where there is plenty of food and not enough means to obtain it; or even where there is plenty to eat, but little is absorbed and retained. Thus the world of hunger is famine in Africa, chronic undernutrition in India, homelessness in Providence, cholera and diarrhea among the poor, and anorexia and bulimia among the affluent.

Incidence

Hunger is often defined as "a compelling need or desire for food." As a need it is measured by diverse concepts of nutrition, energy requirements, or both. As a desire it is described or elicited in personal testimony, including the cries of infants. Or it is implied by food shortage, variably defined.

A glossary of hunger would have to begin with a host of definitions of states of hunger, including nutritional descriptors, such as starvation, undernutrition, malnutrition, dietary deficit, energy-deficient deficit, calorie deficit, chronically inadequate diet, and intake below critical. Food-shortage descriptors include famine, subsistence crisis, food crisis, food insecurity, chronic food insecurity and transitory food insecurity.

Robert W. Kates, PhD, is a University Professor at Brown University and is the founding Director of the newly established Alan Shaw Feinstein World Hunger Program at Brown.

The measurement of world hunger generally takes three forms. That closest to the medical profession relies upon estimates of the numbers of persons affected by symptoms of malnutrition or undernutrition. This form includes direct diagnosis of diseases attributable to protein-calorie malnutrition, vitamin deficiency, and hunger itself, as well as deaths from starvation. Related to these observations, but more indirect, are the various measurements of body weight, height, arm circumference, psychomotor development, and the like.

A second measure attempts to estimate the amount of food consumed and to relate this to estimates of food required to avoid nutritional disease, to undertake certain human activities, or both. The most accurate measure of consumption is the amount of food actually consumed, either directly or as reported by individuals, households, or groups. A more common, but less desirable alternative is the amount of money spent for food converted to food consumption based on typical diets.

The third method, and the one most commonly used in estimating world hunger, is the availability of food in some region, usually by country, compared to some required norm for the population.

None of these methods is satisfactory, nor is their coverage universal. For example, even the least ambiguous symptom, death, receives consistent underestimation by the international rules for classification of causes of death. In cases where malnutrition and infection are jointly implicated in death, the cause is attributed to infection. In

Escudero's words, "The causes for the curious bias of the ICD (International Classification of Diseases), which goes against current knowledge of the malnutrition-infection interaction, lie partly in the convenience of simple explanation and partly in the training of medical professionals, who prefer to explain the world in terms of anatomy and microbes than in terms of food or of sociopolitical systems."[1]

Still less satisfactory are the measures of food consumption and availability. Even in a "tight little island" such as Britain with its long history of social measurements and surveys, depending on the measure of food consumption or availability used, Britons consumed in 1978-80 either 2,240 calories (household consumption survey), 2,900 calories (foodstuffs moving into consumption), or 3,500 calories (FAO* available food supplies) per person per day.[2] Nor is the issue of norms required for life sustenance, growth and development, or various levels of activity satisfactory. The current WHO/FAO† standards are under continual debate, particularly in India, where a contrary "small but healthy" hypothesis has been put forth.[3]

Despite the serious problems with all methods of estimating hunger, estimates are available to bracket the numbers of the hungry world. Grigg[2] recently drew together a number of these statistics for the period around 1980. By updating older figures, he estimates that, if conditions today were similar to the period of these surveys, 130 million children under five and 480 million children under 14 would be suffering from protein/calorie malnutrition.

In general, food availability data calculations, corrected for the disparity of income within a country, yield, depending on the norm used, estimates that range between half a billion and over a billion hungry persons in the world. The most recent World Bank (1986) survey,[4] covering 92 per cent of the developing world, excluding China, concludes that in 1980 340 million people did not have enough income to obtain sufficient energy to prevent serious health risks and stunted growth in children while 730 million had insufficient income to allow an active working life. Of these, about two-thirds of the undernourished live in South Asia and a fifth in Sub-Saharan Africa.

These are measures of chronic hunger worldwide. Recent studies address hunger in the United States. For example, the Physician Task Force on Hunger in America (1985),[5] sponsored by the Harvard School of Public Health, found as many as 20 million hungry Americans.

In a survey of 25 cities, the United States Conference of Mayors (1983)[6] reported that

> Famine, the massive shortage of food affecting large numbers in a region, while attracting the most attention, is less prevalent than chronic hunger. At the current phase of the continuing Sub-Saharan drought, an estimated 19 million people were directly at risk in 16 countries.[7]

Diagnosis

Hunger is a bundle of complex phenomena. One way to simplify these phenomena of hunger is to devise a classification or taxonomy of hunger situations. One generic way to classify hunger is by cause. As a first approach, a proposed threefold taxonomy distinguishes among:

1. Hunger caused by absolute shortage, the unavailability of food within a bounded region because of crop failures, market or transport breakdowns, blockades, or other catastrophes;
2. Hunger caused by poverty, with food generally available within the bounded region, but with affected households unable to pay for food, or have access to resources needed for self-provisioning or both, and,
3. Hunger caused by being deprived of food, generally available to the household, but either intentionally withheld from individuals by custom, abuse, self-denial, or incidentally malabsorbed because of neglect or disease.

The first type, *food-short* hunger, focuses on a larger region or societal grouping; the second, *food-poor* hunger, on the household, while the third, *food-deprived* hunger, focuses on the individual. Thus the taxonomy delineates three different causal mechanisms of hunger and three levels of organization as well. In the last analysis, only individuals suffer the immediate consequences of hunger, but households (broadly defined) are the central organization for food acquisition and redistribution to its members. They draw upon a wider societal or regional foodshed for their need.

The types are not mutually exclusive — food shortage, poverty, and deprivation occur simultaneously in most famine situations. Societies as well as households can be poor or deprived of food and the bounding of a society or region is difficult in an interdependent world where, at

*FAO — Food and Agricultural Organization
†WHO — World Health Organization

Table 1. Changes in the Prevalence of Energy-Deficient Diets in Eighty-Seven Developing Countries, 1970-80

Country Group or Region	Not Enough Calories for an Active Working Life (Below 90 Per Cent of FAO/WHO Requirement)		Not Enough Calories to Prevent Stunted Growth and Serious Health Risks (Below 80 Per Cent of FAO/WHO Requirement)	
	Percentage Change in Share of Population	Percentage Change in Number of People	Percentage Change in Share of Population	Percentage Change in Number of People
Developing countries (87)*	− 6%	+10%	− 2%	+14%
Low-income (30)	+ 4	+41	+ 3	+54
Middle-income (57)	−18	−43	− 9	−44
Sub-Saharan Africa (37)	+ 1	+30	+ 4	+49
East Asia and Pacific (8)	−27	−57	−14	−57
South Asia (7)	+ 3	+38	+ 2	+47
Middle East and North Africa (11)	−25	−62	−14	−68
Latin America and the Caribbean (24)	− 7	−15	− 4	−21

*In parentheses, number of countries.
Source: World Bank (1986, 18)

the largest scale of human organization, there is never any shortage.

Shortage, poverty, abuse and neglect, and disease are immediate causes of hunger. Underlying these are a complex of natural, social, and technological factors that create the paradox of the persistence of hunger in a world of plenty. Advocates and apologists have their pet explanations, but a full sense of the interactions in an interdependent world escapes us. A brief historical perspective, though, may help illuminate the long-term process of coping with hunger.

History

In addition to being a helpful simplification, the concept of food shortage, poverty, and withholding serves as a hypothesis of historical coping with hunger. Over the long span of history, societies seem to grapple first with the prevention of absolute shortage and then more slowly with food poverty. They have barely begun to cope with such problems as intrafamilial access to food, the withholding of food as abuse or torture, the diarrheal diseases in developing countries, and anorexia and bulimia in the industrialized countries.

The struggle to eliminate the extreme food shortages of famine is as old as history. Grain storage, irrigation works, and cycles of plenty and shortage are all described in written records of the earliest civilizations. A recent analysis of climatic disasters in China records 203 events, each of which, mainly through hunger, killed more than 10,000 persons between 180 BC and 1949 AD. By comparison no single disaster in the United States has killed that many people. Only now are the facts emerging about one of the greatest disasters of all time, a famine that may have led to the demise of as many as 34.6 million Chinese.[8]

Absolute shortage of food over large regions seems to have been endemic in the world up to 1800. In a remarkable book, titled *The Last Great Subsistence Crisis of the Western World*,[9] written by Post in 1977 tells of the "year without summer" — 1816 — following the eruption of Mt. Tambora in Indonesia, when much of North America and Western Europe experienced a food crisis. Unlike the many recurrent crises of the previous centuries, however, cities and nations for the first time successfully undertook extensive measures almost everywhere, including organization of food relief and the importation of grain from Russia and the Baltic States.

By 1850, according to Grigg,[2] Europe had coped successfully with the Malthusian shortage of food and had enough food everywhere to feed all of its peoples. Yet, it would take 100 years, after World War II, until the available food in Europe was reasonably well distributed. And even today pockets of poverty, various forms of abuse and neglect, and some disease, still maintain a low level of hunger within Europe.

In still another example, India seems to have dealt effectively with famine over the last 100 years, but chronic malnutrition affects as many as forty per cent of the Indian population and may be increasing, according to Sen.[11]

Worldwide, there is some progress from the time when Lord Boyd-Orr, the first director of the FAO, attributed "a lifetime of malnutrition and actual hunger" to two-thirds of the world's people. Grigg[2] estimates that in the 30-year period from 1950-1980, the proportion of undernourished in the developing world has decreased from 34 per cent to 17 per cent of the population, despite an enormous increase in world population. The recent World Bank study[4] of hunger from 1970 to 1980, using other criteria, records a drop in the proportion with energy-deficient diets over the decade from 40 per cent to 34 per cent for activity and 18 per cent to 16 per cent for growth-limiting hunger. At the same time, the absolute numbers of people with energy-deficient diets in the developing world rose by 10 per cent and 14 per cent respectively for the two criteria of deficiency. Regionally, the major declines in hunger were in East Asia and the Middle East, with rises estimated over the decade for South Asia and Africa.

Prognosis

Between now and the middle or end of the next century, barring nuclear war, world population will increase to between 8 and 12 billion people (2-3 times the current population) and then will probably level off. What are the prospects for ending hunger in a world of 10 billion people?

This is the central question that concerns the newly created Alan Shawn Feinstein World Hunger program at Brown University. The Program, which also addresses hunger through information, education, and recognition is studying five major trends that will affect the capacity to end hunger over the next century. These trends reflect changes in demography, resource base, technology, economics, and values as they affect food production, distribution, and consumption worldwide. Special attention will focus on Africa, where the population is expected to increase fivefold over this time period and the population of the continent's country, Nigeria, will exceed the current population of North America or Europe.

The trends are complex. Population increases compound the task of feeding all, but, in some cases, spur peoples and nations toward needed intensification of agriculture. A warmer, somewhat moister world brought about by the increasing levels of carbon dioxide in the atmosphere will be a boon to agriculture in some places and will disrupt it in others. The emerging green gene revolution of biotechnology will surely lead to increased agricultural production, but not necessarily to less hunger. Indeed, depending on how the technology develops and is used, it could increase the number of rural poor. Use of the market mechanism has led to enormous increases in agricultural production in China and can lead to farm bankruptcies and failures in North America and Europe. Freedom from hunger is a slowly emerging human right, but prescriptions for ending hunger are widely different.

Complexity, however, need not breed complacency. The persistence of hunger in a world of plenty is an affront to human conscience and a challenge to science and society. Its ending is a task that still remains.

References

1. Escudero, J. C. (1985) "Health, Nutrition and Human Development," in R. W. Kates *et al* eds. *Climate Impact Assessment: Studies of the Interaction of Climate and Society.* Chichester, U. K.: John Wiley & Sons, 251-272.
2. Grigg, D. (1985) *The World Food Problem 1950-1980.* Oxford: Basil Blackwell.
3. Seckler, D. (1982) "Small But Healthy": A Basic Hypothesis in the Theory, Measurement and Policy of Malnutrition," in P. V. Sukhatme, ed., *Newer Concepts in Nutrition and Their Implications for Policy.* Pune, India: Maharashtra Association for the Coalition of Science Research Institute.
4. World Bank (1986) *Poverty and Hunger: Issues and Options for Food Security in Developing Countries.* Washington: The World Bank.
5. Physician Task Force on Hunger in America (1985) *Hunger in America: The Growing Epidemic.* Middletown, CT: Wesleyan University Press.
6. U. S. Conference of Mayors (1983) *Hunger in American Cities: Eight Case Studies.* Washington, DC: The Conference.
7. United Nations (1986) Office for Emergency Operations in Africa. *Status Report on the Emergency Situation in Africa As of 1 February 1986.* Report No. OEOA/3/8. New York: United Nations.
8. People's Republic of China (1985). State Statistical Bureau. *Statistical Yearbook of China 1985.* Hong Kong: Economics Information and Agency, December.
9. Post, J. D. (1977) *The Last Great Subsistence Crisis of the Western World.* Baltimore: Johns Hopkins University Press.
10. Sen, A. (1981) *Poverty and Famines: An Essay on Entitlement and Deprivation.* Oxford: Oxford University Press.

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

Do You Know an Impaired Physician?

Treatment of physicians for alcohol addiction shows a favorable outcome in 83 per cent of cases, and treatment of physicians for drug addiction has a 95 per cent success rate. More than 70 per cent of the physicians entering treatment return to the active practice of medicine.

The Rhode Island Medical Society Committee on Impaired Physicians, chaired by Dr Herbert Rakatansky, meets monthly. It is a standing committee of the Society charged with "helping physicians whose professional judgments and capabilities are impaired by their difficulties with chemical dependency or other illnesses."

The Committee handles inquiries in *complete confidence.* If you know of a physician who needs an advocate and support in obtaining necessary treatment, please call or write Dr Rakatansky c/o The Committee on Impaired Physicians, Rhode Island Medical Society, 106 Francis Street, Providence 02903 (401/331-3207).

Some People Commit Child Abuse Before Their Child Is Even Born.

According to the surgeon general, smoking by a pregnant woman may result in a child's premature birth, low birth weight and fetal injury. If that's not child abuse, then what is?

AMERICAN CANCER SOCIETY®

There are three ways to bill

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
•
•
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85	Medicare pmt/adj.			45.-	-8.-	47.-
10/10/85	patient pmt.			-7.-		40.-
10/25/85	Medicare pmt/adj.			-28.-	-5.-	7.-
11/10/85	pt pmt.			-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86	Medicare pmt/adj			-26.-	-5.-	807.-
1/17/86		Coord. adj.			-3.-	804.-
2/2/86	Medicare pmt/adj			440.-	250.-	114.-

PLEASE PAY AT LAST AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86 DATE 2/21/86
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

our patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Words are *printed.* You're not judged by someone else's scribbles.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

Patient year-to-date payment totals.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A

STATEMENT

FED I.D. #00-0000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	E O C	DESCRIPTION	CHARGES PAYMENTS AD PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT						
	YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS		PATIENT	INSURANCE
.00	4.00	.00	.00	.00	NEW BALANCE	4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT" NEW BALANCE" SHOWN.

STATEMENT DATE	PATIENT PAY Y T D	ACCOUNT NUMBER	LOCATION CODES
02/21/86	.00	12090	1 OFFICE 2 HOSPITAL IN PATIENT 3 HOSPITAL OUT PATIENT 4 OTHER 5 OTHER 6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

AIM HIGH

A PRESCRIPTION FOR PHYSICIANS

BOTHERED BY:

- ★ Too much paperwork?
- ★ The burden of office overhead?
- ★ Malpractice insurance costs?
- ★ Not enough time for the family?
- ★ No time to keep current with technology and new methods?
- ★ No time or money for professional development?

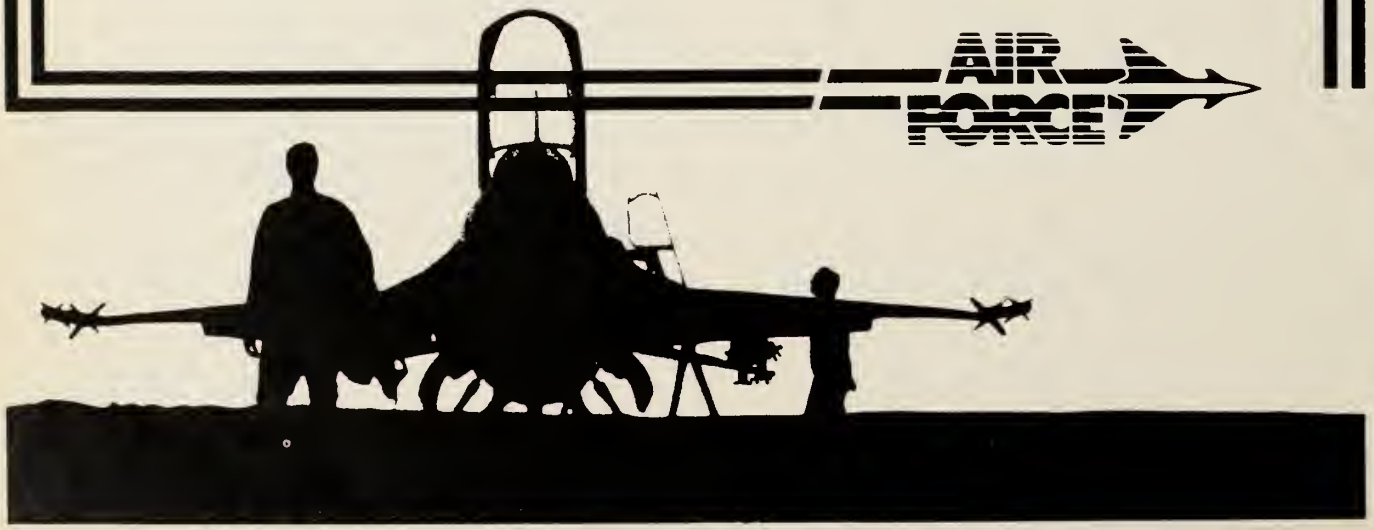
JOIN THE AIR FORCE MEDICAL TEAM; WE'LL PROVIDE THE FOLLOWING:

- ★ Competent and dedicated professional staff.
- ★ Time for patients and for keeping professionally current.
- ★ Financial security, a generous retirement for those who qualify.
- ★ If qualified, unlimited professional development.
- ★ Medical facilities all around the world.
- ★ 30 days of vacation with pay each year.
- ★ Complete medical and dental care.
- ★ Low cost life insurance.

Want to find out more? Contact your nearest Air Force recruiter for information at no obligation. Call

SSgt. A. J. Avila
401-528-4044 collect

AIR FORCE



Traditional Cambodian Health Beliefs and Practices

Understanding Cambodian Traditions Will Facilitate Their Care in a Western Setting

Louise Aronson, BA

Over 110,000 Cambodian refugees have come to the United States since 1975. While Cambodians are the smallest of the Southeast Asian (SEA) refugee groups in the US, they account for almost half of Rhode Island's SEA population (approximately 5,600 of 11,600). In terms of health care, their numerical preponderance is compounded by tendencies for Cambodians to be at greater risk for illness than other SEAs and to rely more on American institutions and individuals for help.[1,2] These tendencies are attributable to their more recent arrival, the huge losses of family and friends suffered by most Cambodians, and the high levels of trauma and physical disability they experienced during the repressive Pol Pot regime. These factors together have created both greater need for help amongst Cambodians and fewer resources for securing it.

This paper surveys the meanings, institutions, and practices of the traditional Cambodian health care system. Although the health beliefs and practices of Cambodian refugees are no longer exclusively traditional, their traditions guide both their responses to illness in the US and the way they adapt to American medicine. I obtained my information from area studies of Cambodia, recent publications of refugee health beliefs and behaviors, and personal interviews with Cambodian refugees.

Louise Aronson, BA, graduated from Brown University in 1986 and is currently completing the Bryn Mawr Post-Baccalaureate Pre-Medical Program.

Introduction

Most Cambodian refugees are from rural regions in a tropical, developing country. They were subsistence farmers and had little education or exposure to Western beliefs and material culture. They left Cambodia to escape oppressive governments, starvation, and war. Their departure was unplanned; they fled to survive. Consequently, they were unprepared for the environments in which they were relocated.

In traditional Cambodian medicine, herbal remedies, dermal techniques, and exorcistic rituals are the principal forms of treatment of illness. When sick, an individual first consults family members. In rural areas of Cambodia prior to the communist takeover, if home remedies were not successful, or if the problem was acute or the onset sudden, traditional healers called *Krou Khmer* were consulted. In most cases, many different treatments and healers were used simultaneously. Western medicine was used by farmers only when all else had failed, and often then it was too late. Consequently, bio-medicine was associated with death in the minds of most rural Cambodians. The same basic patterns of illness behavior were followed by city dwellers, but traditional healers were used less and Western medicine was used more than in rural regions. Still, as is often the case in developing countries, Western medicine was seen as a supplement to and not a substitute for traditional

health care, as but one of many options in a pluralistic system.[3,4]

Cambodian Perceptions of Illness

As is common in many folk medical traditions, Cambodian (also known as Khmer, after the principal ethnic group) understanding of health and disease is not governed by a dominant perspective in the way that Western medicine is centered around the biomedical model. Whereas Western medicine approaches illness from an ontological perspective, Cambodians view disease as an abnormal, imbalanced state induced by either the natural or supernatural environment. Though the Khmer health system recognizes several of the vital organs, human anatomy and physiology in the Western medical sense are not understood. Instead of attributing illness to biological disorder, Cambodians think that metaphysical and supernatural entities determine an individual's health status. Offended spirits, moral transgressions, diet or behavior-induced humoral imbalances, and sorcery are common causes of illness in the Khmer belief system.

One of the principal influences on Khmer conduct, behavior, and mentality is Theravada Buddhism.[5] The Cambodian philosophy of life and by extension many Cambodian beliefs about health and illness, are derived from the Khmer interpretation of Buddhist doctrine. The fundamental principle in Buddhism is the law of *karma,* the law of cause and effect. *Karma,* according to classical Buddhism, means action or deed and can be either good or bad. The law of *karma* stresses the impact of an individual's actions on his or her future well-being. It is linked to the Buddhist concepts of reincarnation and merit and sin in that a person's future incarnation depends on how much merit or sin he or she accumulates. Similarly, a person's current situation, including congenital defects, wealth, social status, and health, reflect the good or bad deeds of his or her previous life.

The effect of the law of *karma* on Cambodian perceptions of illness can be illustrated by considering the case of a child born without one of his arms. Khmer Buddhism suggests at least four explanations for the child's defect: the child could have accumulated a great deal of sin in his previous life; he could have committed the bad deed of having caused another person to lose an arm; he could have had his arm cut in an earlier life; or his mother could have laughed at a person without an arm while she was pregnant, which this sin caused her to bear a child with the same defect.

In addition to affecting traditional Cambodian conceptions of the causes of health and disease, Buddhism influences the Khmer attitude toward sickness. Buddhism is "much less a matter of organized and institutional orthodoxy than a state of mind."[6] The Four Noble Truths taught by Buddha are the following: life is suffering; suffering is caused by desire; suffering can be extinguished by eliminating desire; to eliminate desire, one follows the eightfold path of right understanding, right purpose, right speech, right vocation, right effort, right thinking, and right meditation. As a result of these beliefs, suffering is seen as part of the reality of life, accepted as divine punishment for wrong-doing, and therefore not always acknowledged as a symptom of disease.

The Role of Spirits in Illness

Perhaps in response to the Buddhist tenet that suffering is inevitable, animism, sorcery, magic, and certain elements of Brahminism coexist with Theravada Buddhism in Cambodian culture. Belief in spirits and the supernatural provides the Khmer with an immediate means of coping with suffering. When illness and other deleterious daily occurrences cannot be explained rationally, they are seen as involving spirits or black magic. Supernatural forces are considered responsible for misfortune, accidents, certain types of bodily sickness, and insanity. Like all natural forces, spirits can be both good and bad. Good spirits are usually beneficent, but, if their rights are not respected or if they are offended or mistreated, they may cause illness. The number of different spirits recognized by the Khmer is large, but certain types play more prominent roles in affecting people's health than do others.

Neak Tha are guardian spirits which are generally considered benevolent but which are known to be vengeful and easily angered. They protect social groups and not their individual members. Consequently, Cambodians are often afraid of these protector spirits. There is usually, though not always, one and sometimes two *Neak Tha* in each village or community. *Neak Tha* is the spirit of an old man or grandfather and is commonly found in a tree, forest, mountain, river, or rice paddy. People must worship the *Neak Tha* in order to protect themselves from illness and misfortune. When near a *Neak Tha,* in a forest or on a mountain, for example, an individual must not curse or complain and must share whatever is

eaten or drunk with the spirit. When passing an altar, certain behaviors must be observed, and the spirit should be fed at the altar periodically. If these rules are not followed, *Neak Tha* can make people sick with abdominal pain, vomiting, high fever, constipation, and nightmares; and it can make people laugh and cry inappropriately.[7] Sudden deaths, particularly those resulting from broken necks, are usually attributed to *Neak Tha*. Thus, if a person dies or becomes ill shortly after having been near an altar or a place where the spirit is said to reside, the death or sickness is seen as caused by the vengeance of the *Neak Tha*, who must have been in some way offended by the afflicted individual.

Other spirits which can affect a person's health include demons called *Preay,* witches called *Ab,* ancestral spirits, and spirits of individuals who suffered untimely deaths. The *Preay* appear as bodies of light and fly around at night. They can scare people to death or can cause fevers, sleeplessness, and weight loss. The *Ab,* like the *Preay,* are female and appear only at night. The *Ab* makes sick any human being it encounters. Ancestral spirits, by contrast, only cause sickness when they are treated badly or offended by their descendants. If, for example, a man and woman are living together but are not married, or if one member of a married couple is unfaithful to the other, the ancestral spirits will be angered and cause sickness. Very dangerous spirits are those of stillborn children, women in labor, and people whose unexpected death did not permit performance of the necessary Buddhist rituals.

Natural Causes of Illness

Cambodian perceptions of natural causes of illness are based largely on the idea that health can be achieved only through harmony of the body, mind, and environment. Illness, from this perspective, is related less to biological factors than to an imbalance of bodily humors. These humors are considered the fundamental components of human anatomy. The natural environment, not the gods, determines the extent to which the humors are in harmonious equilibrium.[8] In Khmer medicine, there are two related but different conceptions of humors. One resembles the tenets of both Aristotelian and Ayurvedic medicine. The body, and living matter in general, are seen as composed of four elements: fire, water, wind, and earth. Each element is associated with a particular characteristic, heat, wetness, cold, and dryness, respectively. The other humoral belief system, the hot/cold theory, can easily be conceptually classified as an offshoot or subsystem of this one. It has, however, a significance of its own in Khmer culture and is mentioned more often as a reason for ill-health. (By contrast, the relation of the earth humor to disease is not known by any of my informants.)

The humor known as wind (or air) is also seen by the Khmer as an important determinant of health. It does not seem to have an adequate linguistic or cultural equivalent in English. It must not be confused with wind, the type of weather, but should be understood in metaphysical terms as a flowing element of human anatomy. Sickness is often attributed to excess, deficit, or bad wind. Wind is often associated with blood; if a person does not have enough wind, his or her blood does not flow well. A headache can be understood as an accumulation of bad wind or blood in the head. Stomach problems, particularly those involving flatulence, when the abdomen is distended, are attributed to excess wind. A generic use of the term wind often refers to an array of symptoms referred to in Western medicine as the flu.

The hot/cold theory is similar to (and perhaps derived from) the Taoist theory of yin and yang, two complementary but opposite forces. For good health, the Khmer believe that a balance of the polarities of "hot" and "cold" must be maintained in the body. Hot and cold here do not refer to actual temperatures, but to a metaphysical, symbolic power contained in most substances. The inner workings of the body, then, are related to the relative amounts of hot and cold in an individual's diet and environment. The diseased state is the result of an excess of either hot or cold and can usually be traced to diet, since food is the medium through which the humors act. In order to restore health, the sick person must be exposed to or ingest appropriate amounts of items of the opposite quality to that believed to be responsible for the illness. The classification of foods and illnesses as hot or cold, however, does not appear to be universal and consistent. Each person seems to have his or her own idea of what is hot or cold. In general, meats, coffee and spices are hot; rice, eggs, chicken broth, and tea are neutral; and fruits, vegetables, fish, and chicken are cold. In terms of "disorders" recognized by Western medicine, infections, constipation, pregnancy, and fever are considered hot, while allergies, diarrhea, and the post-partum period are viewed as cold.

Traditional Healing Practices

Traditional Cambodian healing practices reflect the systems of belief discussed above. The principal forms of treatment are dermabrasive procedures, therapeutic burning, medication, massage and accupuncture, and magical ritualistic therapies. Selection of a specific type of treatment depends in part on the nature of the illness — its symptoms and duration and in part on the preference of the patient and his or her family. More than one treatment may be used for the same disorder, or an individual may try a number of different treatments in succession until he or she is cured. Unlike in Western societies, where illness is regarded as a personal problem and where professional help is sought fairly soon after the onset of the illness, sickness and healing in Cambodia involve a broad set of social relations. The aid of a health practitioner is sought only after a whole array of other options has been tried unsuccessfully. Family and community are the primary health care givers. Their responsibilities range from diagnosis to treatment and chronic care. The services of an outside healer are requested only for acute and long-term problems and when special powers or knowledge are needed for treatment.

Dermal treatments are used to relieve a group of common symptoms referred to by the name *Khal Chab*. The symptoms are dizziness, blurred vision, cold extremities, nausea, stomach cramps, headaches, difficulty sleeping, some types of fainting, joint and muscle pain, difficulty breathing, diarrhea, fever, colds, and coughs.[9] The selection of dermabrasive procedure depends somewhat on the disorder being treated, but principally on the amount of pain the sick individual is willing to bear. The procedure is performed by a relative, usually a parent or spouse. These dermal practices are based on the Khmer understanding of illness as related to an imbalance of bodily humors. Each technique described below facilitates the release of the excess wind or energy considered responsible for the disorder. Each practice produces changes in the patient's skin rubefaction, bruising, thermal burns. These burns are seen as evidence of the excess and toxicity of heat or wind in the body and of its exit. While Cambodians do not believe that such techniques can cure serious illnesses, they are universally used for symptom relief. If the symptoms do not recur, the illness is attributed strictly to an environmentally induced humoral disorder. If they do recur, the disorder is seen as the result of bad *karma*, spirits, or sorcery.

The dermal procedures of coining and pinching are used for many of the same health problems. While pinching is considered more effective, it is also more painful and so can be tolerated only by strong and stoic individuals. Coining is done by rubbing a smoothed coin forward along the regions where veins are returning blood to the heart. The coin is lubricated with coconut or cooking oil, wax, or Tiger Balm. It is then pressed to the skin and pulled at a thirty degree angle until the area of focus reddens. The number of lines drawn and their location depends on the disorder. Aches, stiffness, and cold extremities are treated by producing two long vertical marks along either side of the spinal cord and then adding other lines at diagonals, often following the pattern of the rib cage. Colds, coughs, and breathing difficulties are treated by making a semi-circle of short markings on the chest. Headaches and generalized discomforts are alleviated by making long marks along the arms. Pinching is performed by squeezing and twisting fingersful of skin in hopes of forcibly drawing out bad wind. Like coining, it may be done on the chest and back, but the neck, base of the nose, and the region between the eyes are also common sites.

Cupping is used to treat headaches, dizziness, stomach pains, and associated problems such as vomiting and diarrhea. In cupping, a cup is either placed over a candle on the forehead or abdomen, or heated and then placed on the skin. As it cools, it contracts and pulls the skin and the bad or excess wind into the cup. The procedure takes between fifteen and thirty minutes and leaves an ecchymotic area on the skin. If the symptom is particularly severe, a small incision may be made prior to cupping to facilitate the drawing out of toxic humors. If cupping is unsuccessful, the patient might try therapeutic burning. Although burning is often used by trained healers to treat convulsions, epilepsy, and various mental disorders, it is also used in families for relief of stomach problems. The burns are created by placing small bits of bark, vegetable fibers, or other relatively slow burning materials on the skin. Because of the size of the pellets, the burns are rarely severe. The danger of this technique from the Khmer perspective is in applying the pellets to the wrong site. The procedure is believed to release energy, so that if burns are made where there is no buildup of energy, the subsequent deficit of energy could do serious injury.

Traditional Healers

If treatment with dermabrasive techniques and by regulation of the hot/cold balance is unsuccessful, or if sudden or acute illness suggests the influence of supernatural forces, traditional Cambodian healers called *Krou Khmer* are consulted. The word *Krou* means teacher, a wise and knowledgeable person. Although either men or women can be *Krou,* more are men, and most of the female healers function as midwives. An individual can become a *Krou* in several ways, which depend in part on the type of healer the person wants to become. Knowledge is acquired from a relative, a monk, or a master healer who agrees to share his secrets.

Krou who specialize in supernatural medicine and spiritual healing have often studied with monks, learning the magic words and script which give them special powers. The duration of study is anywhere from six months to several years. Some people believe the ability to be a *Krou* is god-given, while others believe it can be achieved. Not all people who study to be *Krou*, however, are successful. A *Krou* establishes himself or herself by curing people, usually beginning with family members, until he or she has acquired, through rumor, a reputation for being a talented healer. A patient selects a *Krou* largely on the basis of confidence and hearsay. If one Krou finds he or she cannot treat a particular patient, the *Krou* recommends that the patient seek the services of another healer. Often, the decision is mutual, and sometimes the sick person is simultaneously consulting another *Krou.* Traditionally, a *Krou* is not paid for his or her services. Instead the healer is offered food, incense, candles, and other items in accordance with the means of the patient and the success of the treatment.

Most *Krou* are skilled in more than one type of healing and have specialized in particular types of disorders within each of their skill areas. Nevertheless, it is possible to distinguish four principal kinds of *Krou Khmer. Krou Thanam* have diagnostic techniques and treatment practices most closely resembling those of modern physicians. In addition to carefully observing the physical and social environments of the patient, these healers read pulses, do abdominal palpations, and measure the strength of the patient's breath. Treatment is sometimes given by the burning techniques described above or by blowing along the person's skin in hopes of removing bad humors. Medication is the most common type of treatment given by the *Krou Thanam.* Most of the medicines come from plants, though some are of animal or mineral origin. Much of the medicine is prepared by decoction or by infusion in water or rice alcohol and administered orally on a regular schedule. Others, especially those fixed to treat superficial wounds, abscesses, and infections, are given in ointment form. Herbs and roots are minced or crushed and mixed with beeswax or coconut oil.[7] Occasionally, medicines are steamed, and the patient breathes in their effects. As there are many different types of herbal medicines, *Krou Thanam* usually specialize. Subspecialties include debilitating diseases, illnesses caused by poisoning, and bone problems.

Another type of *Krou* is the *Krou Banebat,* a healer who diagnoses and treats through meditation and incantation. This type of healer mediates between the natural and supernatural worlds. He is often also a monk or, at least, received his training from monks. Patients come to him when they want to know the ultimate cause of the disorder. He communicates with the spirit world, discovers the source of the illness and talks to the spirits on the patient's behalf. Often the patient and his or her family are instructed to perform a particular rite and to make offerings to the offended spirit. Residual elements of Brahminism are evident in the function of the *Krou Banebat.* This healer serves also as an astrologist, making predictions and diagnoses according to the patient's birthday and the forces of the planets. If the patient is in an astrologically good phase of his or her life, the sickness will probably be cured. If not, the result could be death.

The work of the *Krou Robien* (or *Ibien*) is similar to that of the *Krou Banebat.* He is not a healer, but can influence people's health by making protective amulets and tattoos for them. Such talismans are inscribed with magic formulae and offer protection from both natural and supernatural dangers. A person who has offended a particular spirit might seek the aid of the *Krou Robien* in order to avoid painful repercussions for his deed. Soldiers have traditionally relied on this type of *Krou* to provide them with amulets, which make their skin impervious to bullets and swords.

The fourth major type of *Krou Khmer* is the *Krou Thmop.* He specializes in the treatment of diseases caused by black magic and certain evil spirits. He aims to counter the evil spirit possessing the patient and making him or her sick. The sickness and the evil spirit are attributed to the sorcery of the *Thmop.* Description of *Thmop* is inconsistent both in the literature and between

individuals with whom I have discussed the topic. It seems to be both, or alternately an evil spirit and a sorcerer, a *Krou* gone bad. A person who is angry or jealous of another person can go to a *Thmop* and ask him to bring suffering on the hated person. The victim, in turn, consults the *Krou Thmop* in order to rid himself or herself of the evil spirit. Treatment by this sort of healer resembles somewhat the treatment given by *Krou Banebat* in that both uses rites and incantations. It is often administered when someone suddenly and for no explicable reason begins behaving unusually. The spirit is exorcised with magical incantations and the spraying of water made holy by the words of the *Krou.*

Commentary

The Cambodian perceptions of illness and traditional treatment practices described above are part of an ancient and complex medical system. Belief in bodily humors, *karma,* and spirits is still the norm amongst Cambodian refugees in the United States. Traditional beliefs affect their understanding of biomedicine and the way they respond to illness, health care providers, diagnoses, and treatments. Traditional healing practices, by contrast, are much less easily maintained in a physically and culturally new environment. Herbal remedies, for example, cannot be given if the required substances are not available to make them. Nevertheless, traditional cures and the treatment methods of *Krou Khmer* contribute to the attitudes and expectations of Cambodian refugees in their interactions with the American health care system.

American health care givers can do much to improve the appropriateness of health care for refugees (and therefore to the success of prescribed treatments) if they have some understanding of the refugee mindset and expectations. Many traditional beliefs and practices can be maintained without ill effects by a person receiving Western medical care. Indeed, the refugees are accustomed to medical pluralism. Certainly, the acknowledgement of their medical system by Americans would contribute much toward Cambodian acceptance of American medicine.

References

[1] Moon, A. and N. Tashima. "Help Seeking Behavior and Attitudes of Southeast Asian Refugees. San Francisco: Pacific Asian Mental Health Research Project, 1982.

[2] Mollica, R., G. Wyshak, R. Coelho, and J. Lavelle. "A Psychiatric Patient Treatment Outcome Study." Brighton, Mass: Indochinese Psychiatry Clinic, Department of Psychiatry, St Elizabeth's Hospital, 1985.

[3] Steinberg, D. *Cambodia: Its People, Its Society, Its Culture.* New Haven: Human Relations Area Files Press, 1959.

[4] Whitaker, D. *Area Handbook for the Khmer Republic.* Washington, DC: US Government Printing Office, DA Pamphlet 550-50, 1973.

[5] Sam, Y. "Changes in Khmer Buddhism from 1954 to 1984." Unpublished. Research project sponsored by the Social Science Research Council, Indochina Studies Program. Completed 1985.

[6] Hoang G. and R. Erickson. "Guidelines for Providing Medical Care to Southeast Asian Refugees." *JAMA,* Vol. 248, No. 6, August 1982.

[7] Cambodian Women's Project. "Cambodian Mental Health: A Day to Explore Issues and Alternative Approaches to Care." Conference Proceedings. New York: American Friends Service Committee, May 1985.

[8] Mueke, M. "In Search of Healers: Southeast Asian Refugees in the American Health Care System." *West J Med,* Vol. 139, No. 6, December 1983.

[9] Ros, T. "Coining." Khmer-American Health Newsletter. Hartford: Khmer Health Advocates Inc., Summer 1983. □

A Nursing Home
Striving to Provide
The Ultimate in Nursing Home
Service

100 Wampanoag Trail East Providence
401/438-4275

Health Care — 1986-87

"It Was the Best of Times,
It Was the Worst of Times"

H. Denman Scott, MD

"It was the best of times: It was the worst of times. It was a time of wisdom and a time of foolishness." Had Charles Dickens been writing today, he might well have started a novel on the contemporary health-care scene with these famous lines. In many ways it is the best of times. We have made giant strides in extending life. Since the beginning of this century to the present the death rate has been cut in half. To illustrate this point in another way, in 1900 there were 440,000 residents in Rhode Island, 8,800 of whom died. By 1980 there were 950,000 people in the state, 9,200 of whom died — roughly the same number of deaths, but among more than twice the number of people. The rate of dying dropped among the old, the middle aged, and the young, especially the young. More than 3,000 children under the age of five died in 1900; only 160 in 1980.

This paper formed the basis of an address to the Annual Meeting of the Hospital Association of Rhode Island, November 21, 1986, Newport, Rhode Island.

H. Denman Scott, MD is Director of the Rhode Island Department of Health, Providence, Rhode Island.

The Best of Times

In the early part of the century much of the gain occurred as a result of reduction in poverty and ignorance and the implementation of public health measures related to sanitation, sewage management, and improved nutrition. Then in the late 1930s and the 1940s the sulfonamides, streptomycin, and penicillin were developed. These powerful fruits of biomedical science became widely available to the population, which resulted in a remarkable reduction in mortality from tuberculosis, influenza, pneumonia, and diarrhea/enteritis. New vaccines against tetanus, diphtheria, and whooping cough made mighty contributions toward the control of these serious diseases of childhood.

Beginning about 1950 the decline in the death rate leveled and remained on a plateau until the late 1960s, when it again resumed — a trend which continues to the present day.

While control of the infectious diseases was responsible for the improvements in the first half of the century, prevention and management of the chronic diseases contributed to the reduction in mortality in the latter half. In the past 15 years deaths due to heart disease have fallen by 30 per cent and deaths due to stroke by 42 per cent — a phenomenon which has evoked surprisingly little public notice.[1]

Many factors have contributed to these most promising improvements. First, many of us have heeded advice to eat less fat and cholesterol, to stop smoking cigarettes, and to exercise regularly. The impact of changing our habits is now being documented in studies which show not only that there is less dying as a result of stroke and heart attack, but also that there are actually fewer strokes and heart attacks taking place.[2] In short, preventive behavior pays off for many. Medical care has also played an important role. By virtue of expanded private health insurance and the passage of Medicare and Medicaid, millions of Americans gained access to burgeoning medical skills. These include pharmacologic control of hypertension, emergency resuscitation of heart attack victims, meticulous monitoring in coronary care units, and diagnostic and therapeutic interventions in cardiac catheterization laboratories and cardiac surgical suites. Moreover, we are on the threshold of introducing techniques which promise to revolutionize further the management of heart attacks. Genetic engineering has produced a substance which actually dissolves clots which occur in coronary arteries. If given early after the onset of a sudden occlusion, blood supply is restored to the endangered heart muscle before it dies. However, there is a problem. After the effects of the medicine have worn off, a new clot often occurs at the same point of narrowing in the coronary blood vessel. With coronary angioplasty cardiologists are now able to squeeze the fatty plaque in the blood vessel and expand its lumen. After this procedure the chances of a new clot forming at the site is reduced considerably. Within the next several years the clinical trials that are testing these techniques will be completed and recommendations will be forthcoming about when to use them. These exciting developments will likely benefit several million Americans over the next decade.

Notable strides have also been made in coping with the disabilities of many chronic diseases. Life is not only extended, but its character and quality are improved. Victims of arthritis are now playing tennis on artificial hip joints. Many people severely limited by angina have resumed vigorous lives after coronary bypass surgery. The ability of the lay person to monitor blood sugar in the home is helping diabetics achieve better control and feel more energetic. Cataract surgery and lens implants are restoring vision to thousands. Synthetic vascular grafts are returning circulation to starved leg muscles which could not carry a person more than a few paces. A variety of medications is affording great relief to sufferers of arthritis, asthma, depression, ulcers, and skin disorders.

Progress is also being made against cancer. We are learning in quantitative terms the proportion of cancers related to smoking, alcohol, sunlight, viruses, and diet. We are also gaining insights into occupational and environmental cancers related to certain chemicals, asbestos, and radiation.[3] This knowledge will guide us in the design of educational programs and suggest statutory initiatives which can prevent the onset of various cancers. Advances in therapeutics have been substantial. Several childhood tumors are now regularly cured. Much is also being done to relieve pain and to augment functional capacity.

With such success in the present and with such hope in the future, why are we also in the worst of times? For this there are several reasons.

1. *The disease burden is changing. Many of the new problems have no immediate prospects for biomedical solution or amelioration.* These include acquired immune deficiency syndrome (AIDS) among young adults. By the end of 1991, five years from now, there will have been 270,000 cases of AIDS in the United States, with 74,000 cases occurring in 1991 alone. In the same interval 179,000 people will have died of the disease, 54,000 in 1991. The latter figure approaches the number of combat deaths suffered in the Vietnam War. This scourge will not spare Rhode Island. We shall see well over 1,000 cases in the next five years. In this state during this period more people will die of AIDS than will die on the road in automobile accidents.

While there is some uncertainty in these numbers, they are not wild guesses. The estimates, initially formulated by the United States Public Health Service, have been judged reasonable by an independent panel of the National Academy of Sciences.[4]

Among the elderly, brain failure secondary to Alzheimer's disease has become fearfully common. As we survive the hazards of younger life, more and more of us graduate to the ranks of the very old, among whom this disease is most prevalent. In Rhode Island the number of people 85 and older swelled by 54 per cent from 1970 to 1980. Moreover, this group grew more rapidly than any other age category. Not surprisingly, our requirement for nursing-home beds has expanded. Of the nearly 10,000 nursing-home residents, about half suffer from Alzheimer's. It is estimated that another 2,500-3,000 persons have less severe forms of the disease, but do not yet

require nursing home care. And there inevitably will be many more victims of this disease long before there is any realistic prospect for medical control or cure.[5]

The very old also fall victim to multiple disabilities: vision fails as a result of retinal degeneration, hearing declines, balance becomes impaired, bones become brittle, and joints stiffen and become less mobile. Together these problems make the elderly highly vulnerable to trauma, such as hip fracture and spine collapse, and can render them functionally unable to carry out many of the simple routines of daily life. These frailties are commonly compounded by living alone for long periods.

2. *The importance and value of preventive behavior have only motivated a modest proportion of our population,* chiefly among the well-to-do and the well educated. While millions have managed to stop smoking, almost one-third of us still smoke cigarettes. The evidence is quite convincing that this habit currently accounts for 350,000 premature deaths per year. Cigarettes also are responsible for a substantial proportion of low-birth-weight infants[6] who are susceptible to potentially serious health and developmental problems.

Concerning breast cancer, the message is not yet widely perceived that timely mammographic examination can save 30 per cent of the women who die from this common malignant tumor.[7] Currently, less than 15 per cent of women receive this examination according to the latest guidelines.

Another important failure has been our inability to convince people about the importance of seatbelts. While some progress has occurred at the national and state levels, far too many people lose their lives or sustain serious injury unnecessarily.

3. *Technology, a benefactor so often, is sometimes a tyrant.* People feel trapped by it, particularly at the end of life when multiple life support systems continue to maintain bodily functions long after hopes for decent life have vanished. Many consider such predicaments inhumane and contrary to their religious beliefs which reconcile the mysteries of life and death. In October 1986, in an op-ed piece in the *New York Times,* Doctor Alvan Feinstein, a Professor of Medicine and Epidemiology at Yale, lamented these circumstances which entrapped his own mother and left her in a vegetative state for the two years before she finally succumbed at age 96.[8] I still vividly recall an episode from my house-staff days at the Massachusetts General Hospital. A young woman with end-stage breast cancer experienced a respiratory arrest. I had the duty of inserting an endotracheal tube to gain control of her breathing. As I prepared to insert the tube, she whispered a plea to let her die. I ignored her, stabilized her breathing, and gave her another pain-racked week before all of our ministrations failed and she insisted on dying in spite of us.

These examples illustrate that we are in an era in which decisions to use technology are much easier to support than decisions to withhold it. There is a sense that we will be less harshly judged for doing something rather than not doing something.

4. *The engine of health care now consumes 420 billion dollars, nearly 11 per cent of our gross national product.* This phenomenon has produced much teeth gnashing in many quarters. Should we put additional regulatory brakes on? No, say many. The cry now is "down with regulation. Let the competitive juices flow and do their magic in the market place." In the wake of this relatively new movement, we see the emergence of multi-billion-dollar health-care corporations, mergers, and more mergers. Bigness is in. Health economist Paul Ellwood predicts 10-15 "supermeds" will be caring for almost 50 per cent of the nation's people in 10 to 15 years.[9] These changes are putting enormous strains on doctors, hospitals, administrators, indeed all involved in health care. The climate is often petulant. In the midst of all this, what are we to do about the 30 million uninsured or poorly insured? What are we to do about medical education, and the doctor surplus? What are we to do about the many bankruptcies which occur among the elderly on the way to Medicaid eligibility for nursing-home care? What are we to do about bigness in a little state like Rhode Island?

The problems with which we must cope I find fascinating and energizing. In one way or another we shall all be stretched to our limits. If we stick with the tasks at hand, we shall make progress, create some new history, and leave a legacy of renewal and hope to our successors.

Let us reflect broadly on a few central themes which may guide us through some of these tough problems.

Disease Trends

AIDS and the diseases of aging have to rely on coping skills. Much of the medical and hospital establishment has to re-discover or re-invigorate these capacities, because many professionals have become used to the quick fixes

engineered by the biomedical sciences. This does not mean that medical and surgical therapies, wisely used, have no role in these diseases. They clearly do. There are not, however, any interventions which will either prevent or substantially alter the natural history of these diseases for the better.

With an expanding number of people with intractable and long-term disabilities, we urgently need organizations which can give needed care in a timely fashion, whether it be provided by a doctor, nurse, or some other health professional. Whenever feasible, care and support should be in the home. In today's environment people with money can knit together a reasonable package of care. People without money are in trouble. Many, I suspect, land unnecessarily in hospitals and nursing homes. I do not believe that we shall see any solution until we have a single insurance program which addresses all the needs of the elderly from home care to hospital intensive-care unit. As a first step, that part of Medicaid which deals with the elderly should be incorporated into Medicare. I believe a system can be designed without breaking the bank. We shall soon be developing a more comprehensive statement on this issue.

In summary, health professions must develop new attitudes and renewed patience in dealing with the intractably ill. Organizational entities must evolve to manage the diverse needs of these people. And finally, a unitary system of finance must be created in order to permit the money to flow to the most appropriate level of care.

Prevention

To improve the record of prevention, it is important to understand the attitudes which impede it. Perhaps the greatest psychological obstacle is the fact that we are dealing with "non-events." That person sitting next to you may be alive because he never smoked or because he wore a seatbelt. But who would ever know it? In preventive programs the sense of success comes in watching statistics improve on a graph. Contrast this with the sense of success in watching someone recover in a trauma center from massive injuries suffered in a highway accident. Is it a surprise that the trauma center gets the money while the preventive program often gets lip service?

Some preventive interventions are much easier than others. To prevent measles requires only one decision — an injection early in childhood. To prevent a heart attack requires many decisions, for some even a daily re-dedication, to maintain a proper diet, to refrain from smoking, to exercise regularly, to take the blood-pressure pill. For most of us, such sustained commitment is very difficult indeed. It is especially difficult for those who live in poverty and who lack the durable, caring relationships which are needed to make it through tough times. Unfortunately, most of the preventive mileage has to be made on the difficult side of the course, the one which requires long-term commitment.

Another important consideration is the interval between the initiation of the preventive practice and the point at which the benefit is accrued. A measles shot at age one will usually produce its benefits by age nine or 10; wearing a seatbelt regularly may save your life tomorrow, in 40 years, or somewhere in between; not starting to smoke at age 14 may spare you a heart attack at 50 or a lung cancer at 60.

To the teenage psyche such an interval approaches eternity. For this reason young people commonly discount the danger completely. For most of us there is the tendency to ignore the danger if we are going to encounter the problem some years hence.

This problem is compounded because many of the diseases or injuries we want to prevent are relatively rare and not part of our daily, monthly, or even yearly experience. For example, by age 70, 15 per cent of heavy-smoking men may develop lung cancer, compared to one per cent of non-smoking men. Obviously each smoker is gambling that he will fall into the 85 per cent. What if 75 per cent of heavy smokers developed lung cancer? Surely only a rare lunatic would continue the habit.

To make progress we must understand the psychology involved and devise educational programs that can have impact on both the intellect and the emotions.

Ethical dilemma

Inappropriate life support is not only inhumane and contrary to the patient's wishes, but is also a wasteful use of very expensive resources. I shall never be one to withhold support from someone who wishes to continue the battle. Yet I have a sense of tragedy when "the system" will not let go when the time has come. In my clinical years I faced these moments many times. They are unfailingly arduous and painful for all concerned. The support of family, clergy, and friends is valuable in reaching proper decisions in these difficult circumstances. When such support is lacking, when the doctors and nurses do not know

the patient, when the patient is mentally incapacitated, in these circumstances we often go forward and dedicate our energies to getting one last gasp from the individual.

I, along with many others, applauded the passage of legislation which authorizes a durable power of attorney for health affairs in Rhode Island. This legislation will enable people to designate a trusted relative or friend to make these difficult decisions should the person become mentally incapacitated.

Our job now is to let the people know about this opportunity and ask them to consider taking advantage of it. To this end the Departments of Health and Elderly Affairs will provide the proper forms needed to execute a durable power. However, we need everyone's efforts to get the message to as many people as possible. Persistence in this task will spare many from the trauma of "technologic entrapment."

Health Costs

Affordability

It is improper to address this issue without being mindful of the problems imposed by our huge federal deficits. I have read commentary that we can manage the one trillion dollars in new debt piled up over the last six years; I have heard no one say that we can tolerate the rate of rise in the debt for much longer. Our obligation as citizens must guide our thinking and decisions in the health care arena.

There is always a persuasive case for new and better programs and machines today or next year. I am not advocating deferring any proposals or arguments for them. I do, however, believe that we must somehow continue to wrestle with the issue of affordability. Over the last two years we have made a beginning with the so-called CON-CAP, which defines an annual limit on hospital capital spending. For the first time we have heard the refrain, long familiar to National Institutes of Health applicants, "approved but not funded."

Consider for a moment how we determine whether we can afford something. In the family setting it is a relatively straightforward process — although not necessarily free of vigorous debate. We balance income, need for savings, expenses, and capacity for debt. The process is similar for corporations and for government — for the latter just more complex. Sometime during a year a decision is made with which we must make do — barring major emergencies. Judgments, of course, may be incorrect. Families overspend; organizations go bankrupt; governments badly estimate receipts, expenditures, or capacity for debt.

I cannot extend this thinking to a complex social system such as our health-care enterprise. There is no collective budgetary process or authority which can authorize and appropriate a given level of funding. To some degree, Rhode Island's prospective budgeting program does this in relation to hospital budgets, but this activity relates to only a modest proportion of the health-care dollar. Most of the spending occurs without any budget in mind and is driven by entitlements bestowed by government or by benefits provided in insurance contracts. I am not suggesting we should have a unitary budget for all health care. We must, however, learn to deal with the issue of affordability.

Competition in Health Care

The problem might solve itself if there were numerous competing health plans that both finance and deliver medical care, based on the model developed by health economist Alan Enthoven. In this model, organized medical plans comprise the market on the supply side while individual consumers operate on the demand side.

In the nation, competitive medical plans are growing rapidly and provide care for more than 30 million people, some 13 per cent of the population. In 1985, health maintenance organization (HMO) enrollment grew a hefty 26 per cent. Still, the open-ended fee-for-service mechanisms continue as the dominant form of financing.[10]

What is the situation in Rhode Island? The Rhode Island Group Health Association, a "closed panel" HMO model, has seen its membership grow beyond 70,000. Ocean State Physicians Health Plan, an "individual practice association" HMO model, has reached a membership of nearly 80,000. The various Blue Cross plans still dominate and cover about 500,000 people under 65. Medicare covers 140,000 elderly and disabled individuals, and Medicaid 80,000 low-income people. In many ways we are not unlike the nation as a whole. There is a choice of plans, and there will be more choice to come. Still we have a long way to go to achieve vigorous price competition.

Not to be overlooked are the uninsured. Based on a 1985 Health Department survey of 2,300 Rhode Island households, about 80,000 (8.4 per cent) of its citizens lack health insurance.[11] These are predominantly young people, many of whom are just above the official poverty line and many of whom work only part-time. I do not see much

competition to enroll these people into our health plans.

Can we rely on the "invisible hand" of a market made up of competitive medical plans to produce efficiency and equity to a reasonable degree? Enthoven strongly believes that, left unattended, such a market cannot work unless there is "a carefully drawn set of rules designed to mitigate the market failures endemic to health-care financing and delivery, and without mediation by some form of collective action" on behalf of individuals looking for decent, high-quality health coverage.[9] He argues that health-insurance markets naturally tend to select low-risk individuals, or, if you will, compete for the well and leave the sick for someone else to worry about. He believes that such "market failure" can be controlled or managed by vigilant sponsors of large groups of people, be they employees, the elderly, or the poor. Sponsorship by business, labor, or government requires hard work and continuous surveillance of what is happening to health plan beneficiaries. Tasks for sponsors include: monitoring benefit packages, managing annual enrollments and explaining alternative health plans, insisting on continuity of coverage and stopping exclusions for pre-existing conditions, monitoring disenrollments from individual plans, and assuring that all plans have solid arrangements for high-quality tertiary care. Ultimately, all of these efforts should lead to health plans competing on the basis of solid-quality, cost-efficient medical practice. I urge all in the health-care arena to study carefully what Enthoven has to say.

As I reflect on the concept of managed competition, it appears not to be unqiue to the health domain. There are parallels in the airline industry, the security markets, and other components of our economy. When deregulated, the airlines were allowed to go where they wished and charge what they wanted. But still the Federal Aviation Administration had a major regulatory responsibility. It had to control traffic volume on routes and around airports, and it had to monitor quality and safety maintenance of aircraft. Similarly the Securities and Exchange Commission is exercising its regulatory duty to control the market abuses inflicted by the "inside information" manipulators. So it must be with our health enterprise. I firmly support a vigorous dose of price competition as antidote, in part, to our health cost problems, but only if we have the commitment to be on the lookout for abuses and the will to correct them.

Planning and Certificate of Need

In the weakly competitive market of today we shall continue to need a strong planning and certificate-of-need (CON) capacity. However, if the day of the robust competition were to dawn, should planning and regulation disappear? The "free marketeers" argue for this forcefully, but, in my opinion, not convincingly. For business, labor, or government to be good sponsors, they need advice and counsel which only a community-focused planning capacity can provide. It is important to distill the latest information on preventive medicine and diagnostic and therapeutic technology, and then reflect on when and where these new interventions should be introduced into the state. Thereby will evolve health policy. Such a process should involve the public and private sectors and be open to all points of view.

Once a policy is agreed to, we must figure out how to implement it. This is difficult, and requires a willingness to understand the many practical barriers which must be worked through, and not run over, in order to reach the goal.

Consider the issue of how to deploy the promising therapies of thrombolytic drugs and coronary angioplasty. Because of their enormous potential to salvage and extend many lives, it is logical that we plan to have these capabilities readily accessible to all of our citizens. I do not have a clear idea of what should evolve. We need expert advice and probably several versions of a plan before coming to a reasonable formulation. Because much money and prestige will be involved, the process will not likely be a tidy one. It will witness the expression of much institutional and regional rivalry. A rigorous, data-based exposition of the issues must counterbalance such rivalry and be driven by a ceaseless intent to create a plan which will serve the general interest of the people.

Rhode Island's certificate of need legislation, which in 1968 gave birth to the Health Services Council, arose because of concern about rising hospital costs and the desire to avoid expensive duplication of service. Its emphasis has been primarily on cost containment. As price competition and federal initiatives — such as "diagnosis-related groups" (DRGs) — mitigate the rate of rise in our costs, the CON program should increasingly become concerned with the wise deployment of expensive technology. It should also focus on the potential for the technology to be used according to high professional standards. Excessive zeal to cut prices may compromise quality. Surely we must guard against this.

To achieve quality one needs excellent equipment; well-trained, highly-skilled, personnel; and sufficient patient volume to maintain and improve those skills. Regular review of outcomes and complications is also crucial. Consider again the airline industry. A pilot maintains his skill whether the airplane is full or empty. He needs only an airplane. A surgeon or a cardiologist who performs catheterizations needs patients. Good medicine cannot be maintained in an "empty airplane."

Lack of adequate clinical volume is becoming an increasing problem. This is happening because we are producing more physicians than we need. Also, in certain parts of the country hospitals are starting high-tech programs with no realistic expectation of an adequate case load. For example in Arizona, where the CON laws were repealed in 1985, there has been an explosion of hospital construction and program development. In 1984, before deregulation, there were nine open heart surgery units operating in four hospitals in Phoenix. After deregulation four additional Phoenix hospitals initiated open heart services — all developed under the banner of competition.[12] While we perhaps can afford to see airlines go belly up without any increased danger to people, should the public experience a similar shakedown cruise in the health sector? My response is an emphatic no.

The CON program should also look at new proposals with broader lenses which focus explicitly on the following questions. What is a project's potential to: 1. extend life, 2. reduce disability, 3. augment quality of life, 4. increase service productivity, or 5. produce actual cost savings? While beguilingly simple in one sense, the actual response to these questions will be difficult. It will take time to learn how to ride such a bicycle, but we should begin. There will be further discussion of the CON program. The Department of Health is preparing a paper which will describe the origins of CON, its advantages and disadvantages, its dynamic evolution, and our proposals for its strengthening.

Conclusion

Unprecedented stress is now part of our professional lives. Forces are at work which will alter many traditional arrangements, whether we like it or not. It is hard to know how fast the rate of change will occur. Because much good work still accrues from conventional practices, change will probably come more slowly than many are predicting. The most conservative among us would prefer the course, to use Russell Baker's phrase, "forward to the past." In my judgment this would be unacceptable and leave our health enterprise in Rhode Island in a weakened condition, ripe for takeover by one of the "supermeds." I do not think we want our health care institutions controlled by someone in Beverly Hills or Chicago. To a greater or lesser degree this could happen unless we have the collective will to prune our system and create the circumstances which will promote its healthy growth and development. I have high hopes that we can develop in ways which will allow us to care for not only our Rhode Island citizens but also for many in neighboring states who could look to us for high-quality, cost-effective health care. This has happened already in neonatal care and in certain aspects of cardiology. Surely it can happen in other endeavors.

As the conservative attitudes clash with the forces of change, I am reminded of Robert Frost's poem, "Mending Wall." In it he describes two men who repair a stone wall between their respective properties, damaged by winter storms and frost heave. The conservative of the two reflects on the theme: "good fences make good neighbors." The wall is a barrier in one sense; in another, it promotes harmonious human relations. The other man sees the wall as an unnecessary impediment. "Something there is that doesn't love a wall, that wants it down." He says, "Before I built a wall I'd ask to know what I was walling in or walling out, and to whom I was like to give offense." Frost has captured the essence of our contemporary problem in health care. What walls need to come down, new relationships forged, and, at the same time, how do we remain good neighbors?

References

1 National Center for Health Statistics, *Health: United States 1985.* DHHS Publication No. (PHS) 82-1232.

2 Pell S, Fayerweather WE: "Trends in the Incidence of Myocardial Infarction and in Associated Mortality and Morbidity in a Large Employed Population, 1957-1983." *NEJM,* Vol. 312, No. 16, April 18, 1985.

3 Doll R, Peto R, "The Cancer of Cancers: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today." *J. National Cancer Institute* 66:1191-1308, 1981.

4 Institute of Medicine, National Academy of Sciences: *Confronting AIDS, Directions for Public Health, Health Care, and Research.* National Academy Press, 1986.

5 *Final Report: The Rhode Island Legislative Commission on Dementias Related to Aging, May 1, 1984.*

6 Fiedling JE, "Smoking: Health Effects and Control. *NEJM,* 313:491-498, 555-561, 1985.

7 Tabar L, et al "Reduction in Mortality from Breast Cancer After Mass Screening With Mammography." *The Lancet — Saturday 13 April 1985.*

8 Feinstein AR. *New York Times, Monday, October 6, 1986, page A19.*

[9] Ellwood PC, *The Medical Organization of the Future.* Published by American Group Practice Association, 1422 Duke Street, Alexandria, VA 22314.
[10] Enthoven AC, "Managed Competition and the Unfinished Agenda for Competition in Health Care," (unpublished manuscript)
[11] Rhode Island Department of Health, *1985 Health Interview Survey Report, 1986.*
[12] *American Medical News* — September 19, 1986. □

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY....ANYWHERE

PLUS insurance for....
tax audit
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

A WORD TO THE WHYS

WHY AMA? AMA-sponsored Group Disability insurance is designed to replace a substantial portion of your income should you be unable to practice due to sickness or accident. Unlike many policies, AMA-sponsored Disability Insurance provides benefits if you are unable to perform *your* occupation in *your* medical specialty. Providing you with benefits you can't afford to be without: it's one more good reason why you should be a part of the AMA.

WHY AMA? Now, for the first time there's a forum for hospital medical staffs to meet nationally to discuss common problems and changes in physician-hospital relationships. The Hospital Medical Staff Section was recently created by the AMA to provide leadership in ensuring quality patient care during this period of massive hospital restructuring. It's one more good reason why you should be a part of the AMA.

WHY AMA? Commitment to maintaining high quality at all levels of medical education is one of the AMA's proudest traditions. The AMA creates policy for medical education, participates in accreditation activities, and supplies the public with information on medical education issues. Proven dedication to high standards in medical education: it's one more good reason why you should be a part of the AMA.

To Join, Contact your county or state medical society or write: Division of Membership, AMA, 535 North Dearborn Street, Chicago, Illinois 60610 or call collect, (312) 751-6196.

AMA
AMERICAN MEDICAL ASSOCIATION

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

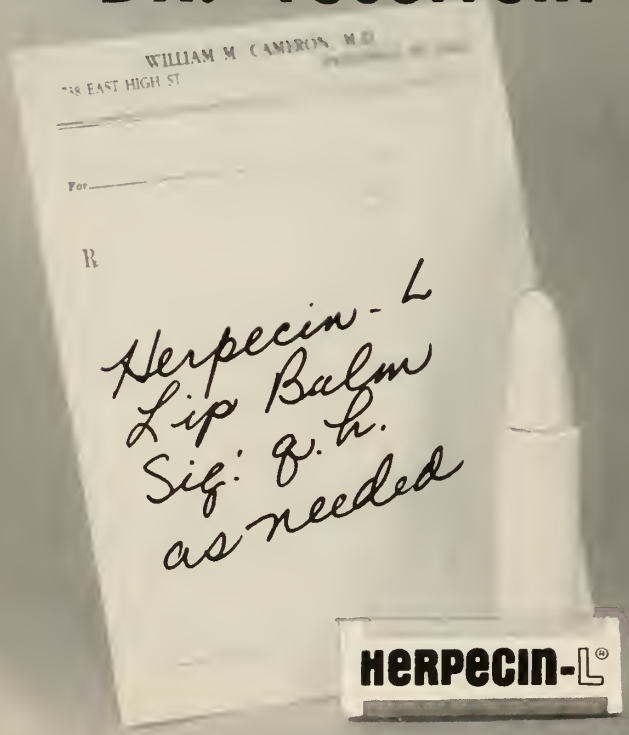
DOCTOR'S OFFICE
EAST SIDE
FOR SALE OR RENT

Large, Modern, Fully Equipped
Plenty of Parking

Large Fresh Modern Apartment
Available Upstairs

401-785-9671
between 8-9:30 pm

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

Motrin® 800 mg TABLETS
ibuprofen

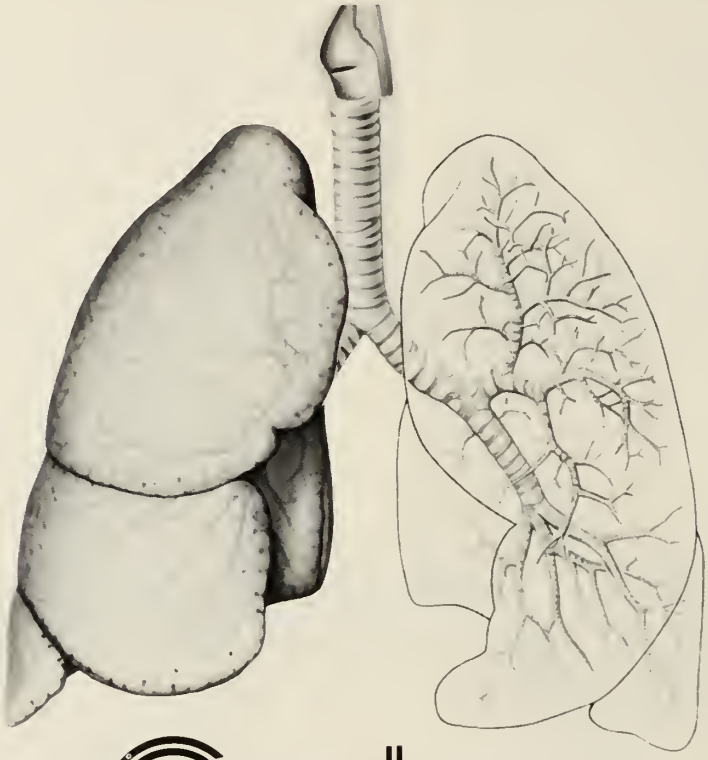
Extra strength
Convenience
Economy

Upjohn 100 A Century of Caring 1886·1986

©1986 The Upjohn Company

J-6138 January 1986

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae*, *H influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Note: Ceclor® is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *S. pyogenes* (group A beta-hemolytic streptococci).

Contraindications: Known allergy to cephalosporins.

Warnings: CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:

- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- In renal impairment, safe dosage of Ceclor may be lower than that usually recommended. Ceclor should be administered with caution in such patients.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:

- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, erythema multiforme, serum-sickness-like reactions): 1.5%; usually subside within a few days after cessation of therapy. These reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children)
- Abnormal urinalysis; elevations in BUN or serum creatinine
- Positive direct Coombs' test
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly)

© 1986, ELI LILLY AND COMPANY [060485LR]

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

Lilly

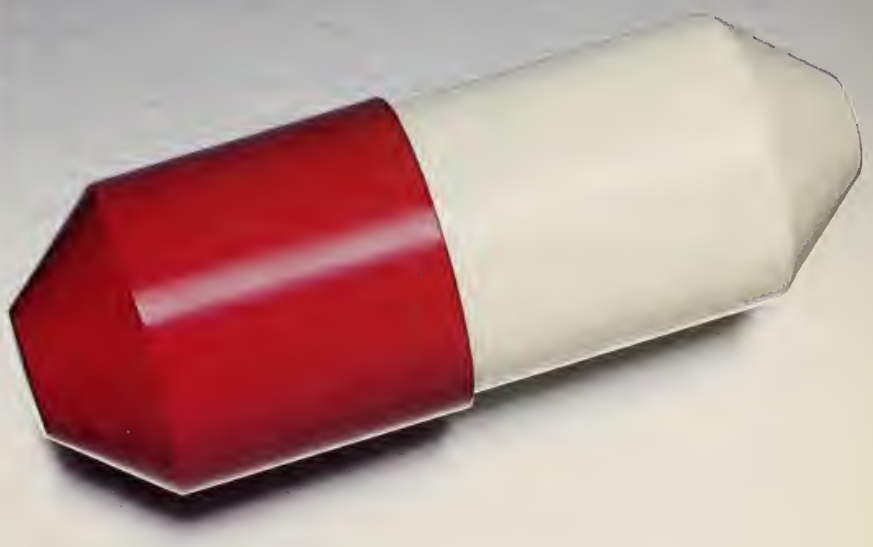
Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

600332

In Hypertension*... When You Need to Conserve K+

Remember the Unique Red and White Capsule: Your Assurance of SK&F Quality

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).



Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ L42

Potassium-Sparing

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Over 20 Years of Confidence

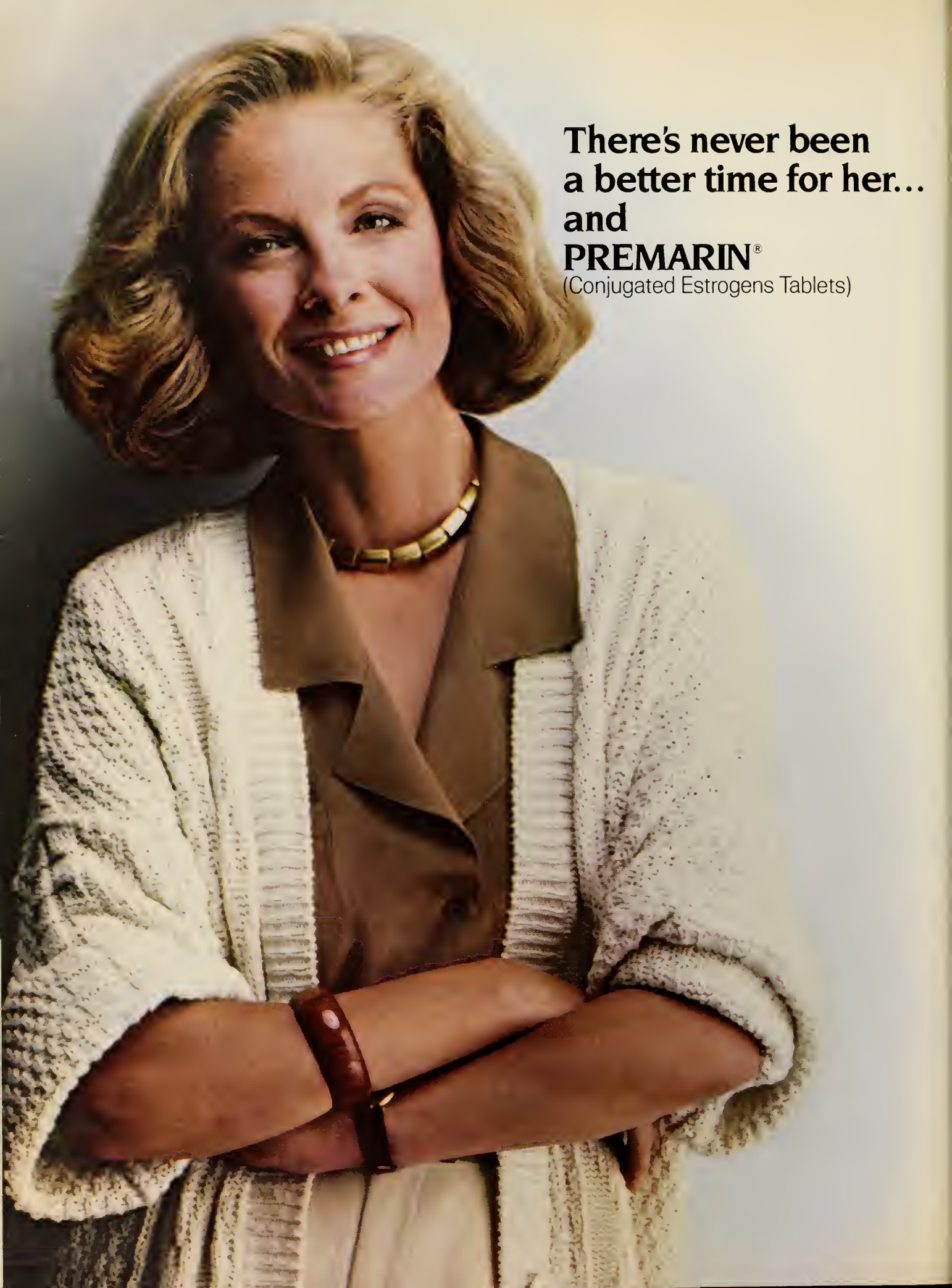
The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

a product of

SK&F CO.

Carolina, P.R. 00630

© SK&F Co., 1983



There's never been a better time for her... and PREMARIN®
(Conjugated Estrogens Tablets)

Now the evidence looks better than ever

Significantly reduced risk of endometrial hyperplasia

Endometrial hyperplasia was significantly reduced when progestin was added to PREMARIN therapy for more than ten days a month.[1-4] The risk of endometrial hyperplasia may also be reduced through cyclic administration of unopposed, low-dose PREMARIN.

Effect on lipids—an important feature

PREMARIN used alone does not adversely affect lipid levels. In fact, a clinical study has shown a significant increase in HDL cholesterol—from 49.7 mg/dL to 56.4 mg/dL—and decrease in LDL cholesterol—from 165.1 mg/dL to 138.1 mg/dL—after one year of therapy with PREMARIN, 0.625 mg.[5]

Low-dose control of menopausal symptoms*

PREMARIN effectively relieves vasomotor symptoms, such as hot flashes. When estrogen deficiency is limited to atrophic vaginitis, PREMARIN® (conjugated estrogens) Vaginal Cream restores the vaginal environment to its premenopausal state.

The most widely used, most extensively studied estrogen worldwide.

PREMARIN®
(Conjugated Estrogens Tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms

PREMARIN®
(Conjugated Estrogens Tablets)

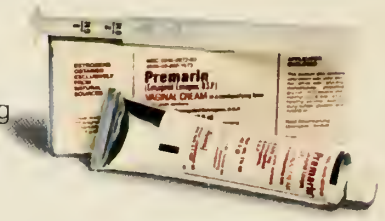
0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(Conjugated Estrogens)

Vaginal Cream
0.625mg/g



BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1 ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2 ESTROGENS SHOULD NOT BE USED DURING PREGNANCY

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP). Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy. (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow, dysmenorrhea; premenstrual-like syndrome, amenorrhea during and after treatment, increase in size of uterine fibromyomata; vaginal candidiasis, change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating, cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum, hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine, dizziness, mental depression, chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term* use *only*. For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically*. Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis —0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Whitehead MI, Townsend PT, Pryse-Davies J, et al: Effects of estrogens and progestins on the biochemistry and morphology of the postmenopausal endometrium. *N Engl J Med* 1981;305:1599-1605. **2.** Paterson MEL, Wade-Evans T, Sturdee DW, et al: Endometrial disease after treatment with oestrogens and progestogens in the climacteric. *Br Med J* 1980;280:822-824. **3.** Magos AL, Brincat M, Studd JWW, et al: Amenorrhea and endometrial atrophy with continuous oral estrogen and progestogen therapy in postmenopausal women. *Obstet Gynecol* 1985;67:496-499. **4.** Whitehead MI, Lane G, Siddle N, et al: Avoidance of endometrial hyperstimulation in estrogen-treated postmenopausal women. *Semin Reprod Endocrinol* 1983;1:1;41-52. **5.** Barnes RB, Roy S, Lobo RA: Comparison of lipid and androgen levels after conjugated estrogen or depo-medroxyprogesterone acetate treatment in postmenopausal women. *Obstet Gynecol* 1985;66:216-219.

© 1986 Ayerst Laboratories

Ayerst® AYERST LABORATORIES
New York, NY 10017

T6194/886

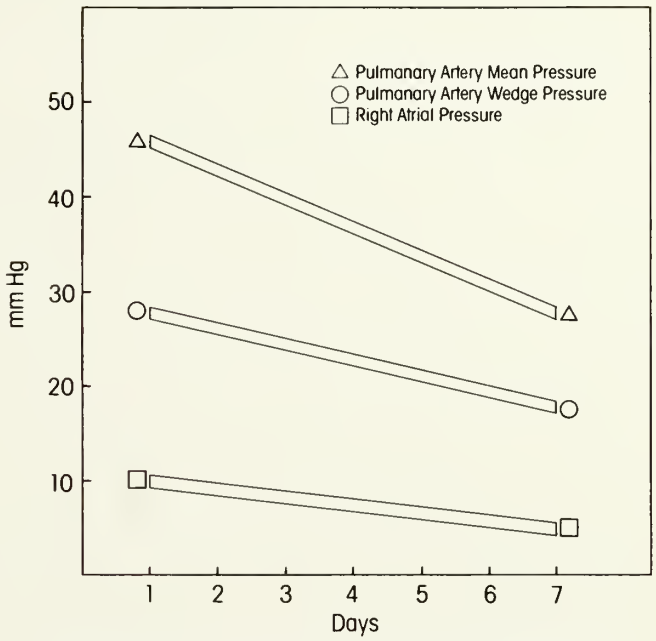
Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml
and 10-ml vials (0.25 mg/ml)

REDUCES FLUID OVERLOAD and eases the burden on the failing heart

Significantly improves hemodynamics



Ten patients with CHF showed marked hemodynamic improvement after seven days of BUMEX® (bumetanide/Roche) (mean values ± SE) Adopted from Olesen, *et al* [1]

References: 1. Olesen KH, *et al Postgrad Med J 51* (Suppl 6) 54-63, 1975 **2.** Hondler B, Dhingra RC, Rosen KM *J Clin Pharmacol 21* 706-711, Nov-Dec 1981 **3.** Broter DC, *et al Clin Pharmacol Ther 34* 207-213, Aug 1983 **4.** Broter DC, Fox WR, Chennovosin P *J Clin Pharmacol 21* 599-603, Nov-Dec 1981 **5.** Davies DL, *et al Clin Pharmacol Ther 15* 141-155, Feb 1974

BUMEX®
bumetanide/Roche
0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)

BUMEX® (bumetanide/Roche)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome
Almost equal diuretic response occurs after oral and parenteral administration of Bumex If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity
CONTRAINDICATIONS: Anuria Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion. Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment
WARNINGS: Dose should be adjusted to patient's needs Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients.
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risks to the patients
In patients with hepatic cirrhosis and ascites, sudden alterations at electrolyte balance may precipitate hepatic encephalopathy and coma Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved The potential for ototoxicity increases with intravenous therapy, especially at high doses
Patients allergic to sulfonamides may show hypersensitivity to Bumex
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets Hyperuricemia may occur Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency Bumex may increase urinary calcium excretion
Possibility of effect on glucose metabolism exists Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics
Probenecid should not be administered concurrently with Bumex
Concurrent therapy with indomethacin not recommended
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage
Interaction studies in humans have shown no effect on digoxin blood levels
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus
Bumetanide may be excreted in breast milk
Pediatric Use Safety and effectiveness below age 18 not established
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease)
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts Increases in urinary glucose and urinary protein have also been seen
DOSAGE AND ADMINISTRATION:
Oral Administration. The usual total daily dosage is 0 5 to 2 0 mg and in most patients is given as a single dose
Parenteral Administration Administer to patients (IV or IM) with GI absorption problem or who cannot take oral The usual initial dose is 0 5 to 1 mg given over 1 to 2 minutes If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day
HOW SUPPLIED: *Tablets*, 0 5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescription Paks of 30, Tel-E-Dose® cartons of 100 Imprint on tablets 0 5 mg—ROCHE BUMEX 0 5, 1 mg—ROCHE BUMEX 1, 2 mg—ROCHE BUMEX 2
Ampuls, 2 ml, 0 25 mg/ml, boxes of ten
Vials, 2 ml, 4 ml and 10 ml, 0 25 mg/ml, boxes of ten

ROCHE®

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc
Nutley, New Jersey 07110

ROCHE

OVERLOAD

Reduce fluid volume and improve hemodynamics in CHF

Edema due to congestive heart failure often demands highly effective diuresis to reduce the fluid load on the failing heart. Bumex® (bumetanide/Roche) is the next generation in loop diuretic therapy for three powerful reasons. It moves out an unsurpassed volume of fluid and sodium, resulting in significant reductions in edema and right atrial and pulmonary artery wedge pressures.[1,2] It's almost completely absorbed through the GI tract, so it's easy to titrate.[3] And Bumex completes high-volume diuresis fast—within four hours at usual doses.[4,5] Your patients spend less time in diuresis, more time in normal activities.

Bumex has a good safety profile; however, as with all loop diuretics, Bumex, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion, including hypokalemia. Serum electrolytes should be monitored periodically, especially in patients on low salt diets or those treated for prolonged periods or on high doses.

Bumex®
bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets, 2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

First line loop diuretic therapy

Please see references and summary of product information on preceding page.

Copyright © 1986 by Hoffmann-La Roche Inc. All rights reserved

Rhode Island Medical Journal

March 1987
Volume 70, Number 3

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
MAR 25 1987

DISPLAY
SHELVES

A Look Into The Physician's Role With The Smoking Patient
(see page 121)

CONTRIBUTIONS

109 **Disseminating Intravascular Coagulation Following First Trimester Abortion in Polycythemia Vera**

113 **A Five Year Review of Hymenoptera Allergy: 299 Patients**

121 **Understanding the Smoking Problem and How to Help Patients Stop: Current Status of the Field**

127 **Dollars and Sense of Percutaneous Biopsy**

107 **EDITORIAL**

101 **INFORMATION FOR AUTHORS**

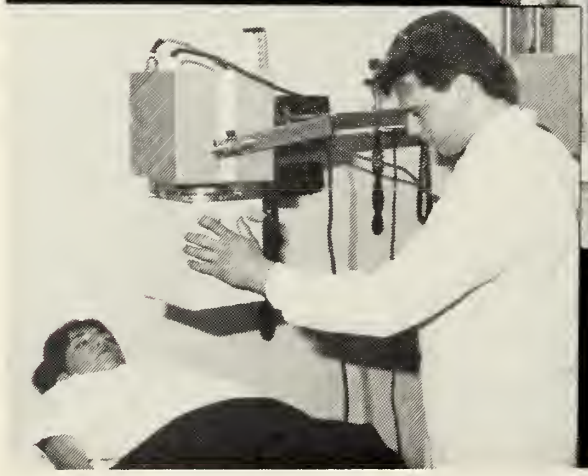
We've become the largest full service medical lab in Rhode Island...*because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011

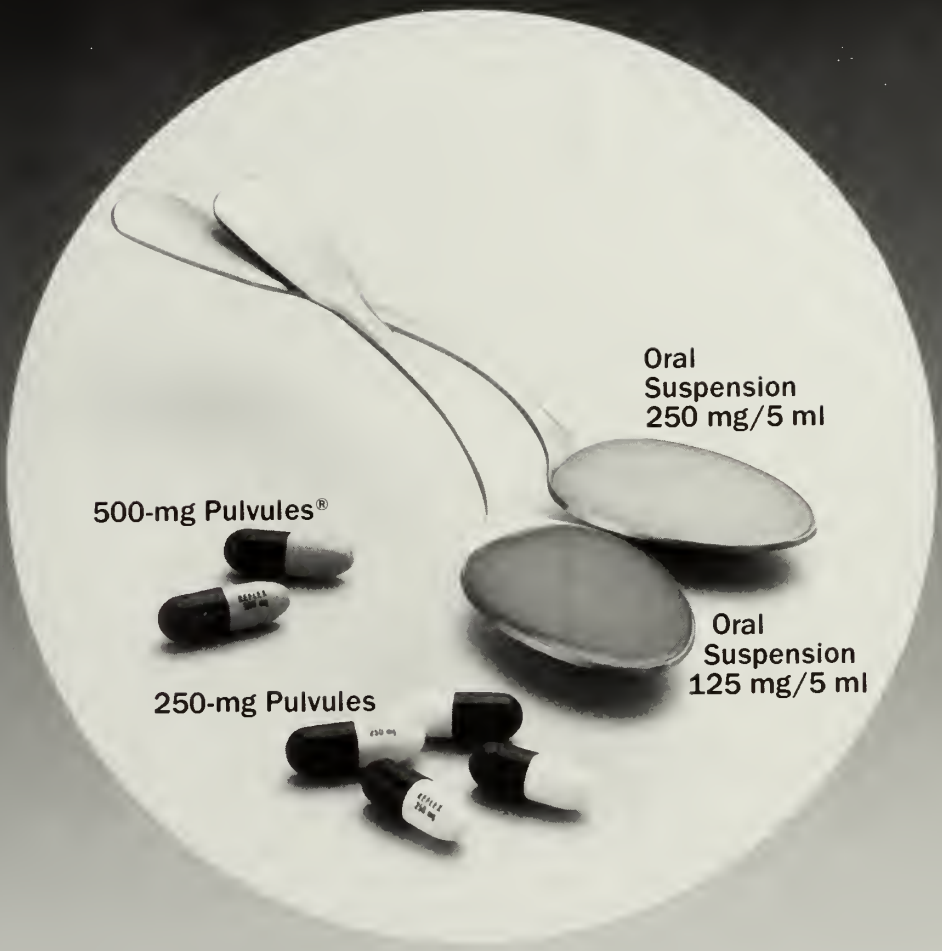


CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry Narragansett • West Warwick • Cumberland

Easy To Take



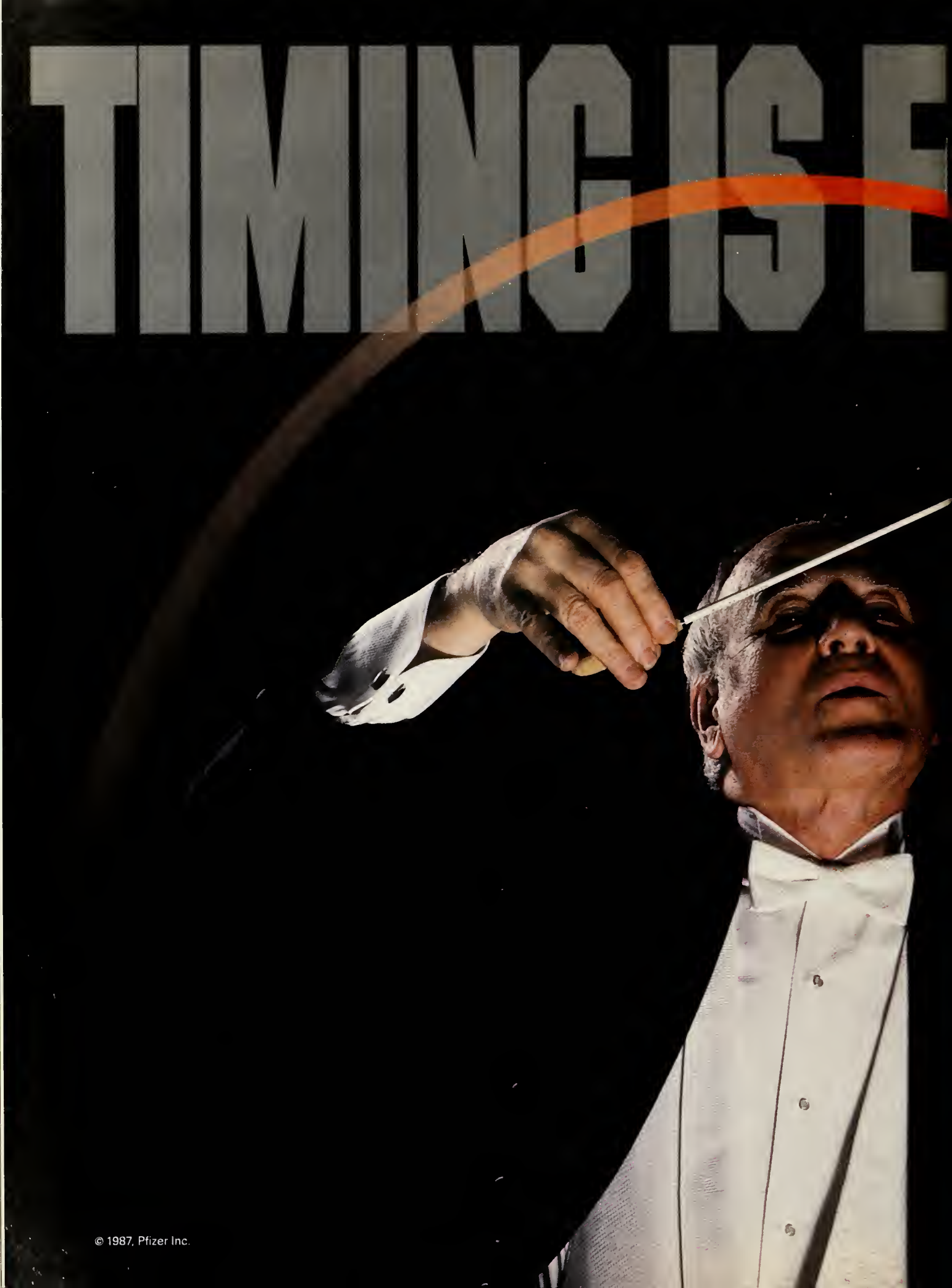
Keflex®
cephalexin

Additional information
available to the profession
on request.

DISTA
420113

Dista Products Company
Division of Eli Lilly and Company
Indianapolis, Indiana 46285
Mfd. by Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

TIMING IS E



© 1987, Pfizer Inc.

VERYTHING

Effective control time and time again[1]

Effective control of fasting and postprandial glucose—patient after patient, meal after meal, year after year.

Insulin when it's needed

Insulin levels are rapidly elevated in response to a meal, then return promptly to basal levels after the meal challenge subsides.

Timed to minimize risks

Rapidly metabolized and excreted, with an excellent safety profile.[1] As with all sulfonylureas, hypoglycemia may occur.

In concert with diet in non-insulin-dependent diabetes mellitus

Glucotrol®

(glipizide) 5-mg and 10-mg Scored Tablets

SYNCHRONIZED SULFONYLUREA THERAPY

Please see brief summary of Glucotrol® (glipizide) prescribing information on next page.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Reference
1. Sachs R, Frank M, Fishman SK. Overview of clinical experience with glipizide. In *Glipizide: A Worldwide Review*. Princeton, NJ: Excerpta Medica; 1984; pp 163-172

GLUCOTROL® (glipizide) Tablets
Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM; type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19, supp. 2:747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur.

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hyperglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly fetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This fetotoxicity has been similarly noted with other sulfonylureas, such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects: Prolonged severe hypoglycemia has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Chloestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas.

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours since hypoglycemia may recur after apparent clinical recovery. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL (glipizide), dialysis is unlikely to be of benefit.

DOSAGE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL, in general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100; 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-65) Bottles of 100.

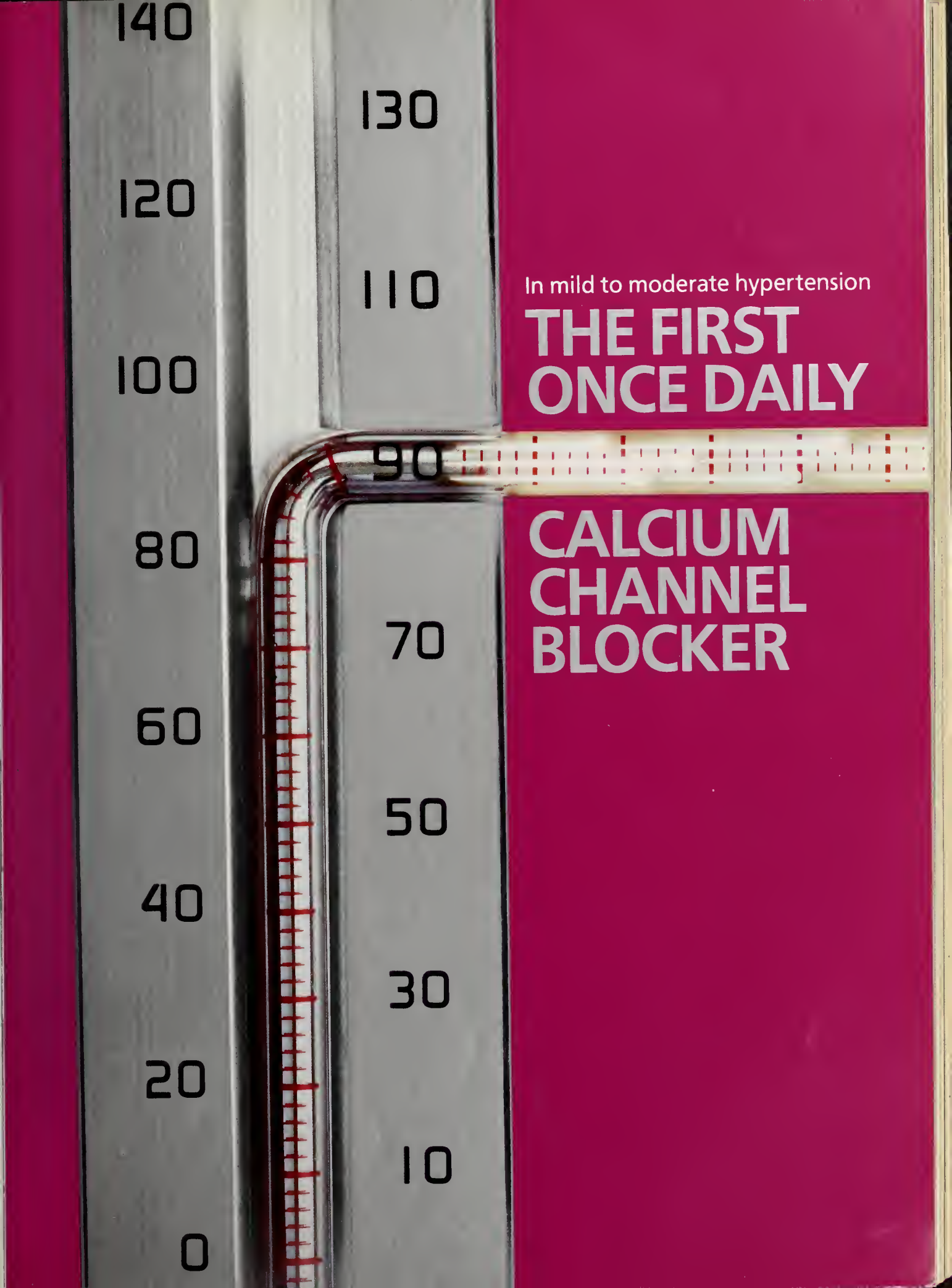
CAUTION: Federal law prohibits dispensing without prescription.

More detailed professional information available on request.

ROERIG Pfizer A division of Pfizer Pharmaceuticals
New York, New York 10017

© The Advertising Council, 1985

A Public Service Message Ad Council U.S. Department of Transportation


140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
In mild to moderate hypertension
THE FIRST ONCE DAILY
CALCIUM CHANNEL BLOCKER

NEW
ONCE DAILY

ISOPTIN SR*

(verapamil HCl/Knoll)

240 mg scored, sustained-release tablets

JAMES B.
38, black male, heavy smoker. Prescribed a diuretic by another physician last year for hypertension.

YOUR CONCERNS
Presents with "smoker's cough." Workup reveals a BP of 150/107.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Black hypertensives often have low plasma renin activity and generally do not respond favorably to beta blockers.
— Beta blockers may increase the likelihood of bronchospasm.

ALICE W.
65, diabetic, overweight. Her BP has elevated to 190/98.

YOUR CONCERNS
She's on daily insulin.

A LOGICAL CHOICE FOR CONTROL OF HER BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike most beta blockers and diuretics, ISOPTIN has no adverse effects on serum glucose levels.
— Unlike most beta blockers, ISOPTIN does not mask the symptoms of hypoglycemia.

THOMAS G.
70, asthmatic. In the past, BP adequately controlled with 25 mg hydrochlorothiazide daily.

YOUR CONCERNS
Today patient presents with symptoms of gout. Workup reveals high uric acid level, low serum potassium, and BP elevated to 180/98.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN will not decrease serum potassium levels or elevate uric acid levels.
— Unlike beta blockers, ISOPTIN can be used safely in asthma and COPD patients.

JOHN K.
42, Annual physical uncovered diastolic BP of 102... confirmed on three successive office visits. Unresponsive to nonpharmacologic intervention.

YOUR CONCERNS
Salesman, spends many hours of his working day in car... total cholesterol level 300, HDL 35.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN does not cause urinary urgency.
— Unlike either beta blockers or diuretics, ISOPTIN will not adversely affect his already seriously compromised lipid profile.
— Unlike with propranolol, fatigue and impotence are rarely reported.

Antihypertensive therapy you and your patients can live with

*A product of Knoll research.

© 1986, BASF K & F Corporation

2538/1-87

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

BASF Group

knoll®

Printed in U.S.A.

In mild to moderate hypertension

Brief Summary

THE FIRST ONCE DAILY CALCIUM CHANNEL BLOCKER

ISOPTIN® SR
(verapamil HCl/Knoll)
240 mg scored, sustained-release tablets

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS), 2) Hypotension (less than 90 mmHg systolic pressure) or cardiogenic shock, 3) Sick sinus syndrome or 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker).

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction (see DRUG INTERACTIONS). Patients with milder ventricular dysfunction should, if possible, be controlled before verapamil treatment. Hypotension: ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension. Elevated Liver Enzymes: Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with paroxysmal and/or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil. While this has not been reported with oral verapamil, it should be considered a potential risk. Treatment is usually D.C.-cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block, while infrequent (0.8%), may require a reduction in dosage or, in rare instances, discontinuation of verapamil HCl. Patients with Hypertrophic Cardiomyopathy (IHSS): Although verapamil has been used in the therapy of patients with IHSS, severe cardiovascular decompensation and death have been noted in this patient population.

PRECAUTIONS: Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted in the urine. In patients with impaired hepatic or renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDOSAGE).

Drug Interactions: Beta Blockers: Concomitant use of ISOPTIN and oral beta-adrenergic blocking agents may be beneficial in certain patients with chronic stable angina or hypertension, but available information is not sufficient to predict with confidence the effects of concurrent treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities. Digitalis: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment increases serum digoxin levels by 50 to 75% during the first week of therapy and this can result in digitalis toxicity. Upon discontinuation of ISOPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antihypertensive Agents: Verapamil administered concomitantly with oral antihypertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, beta blockers, prazosin) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Disopyramide: Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration. Quinidine: In patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. There has been a report of increased quinidine levels during verapamil therapy. Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Two clinical trials have shown a lack of significant verapamil interaction with cimetidine. A third study showed cimetidine reduced verapamil clearance and increased elimination to 1/2. Anesthetic Agents: Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics. Carbamazepine: Verapamil may increase carbamazepine concentrations during combined therapy. Rifampin: Therapy with rifampin may markedly reduce oral verapamil bioavailability. Lithium: Verapamil may lower lithium levels in patient on chronic oral lithium therapy. Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no evidence of a carcinogenic potential of verapamil administered to rats for two years. Verapamil was not mutagenic in the Ames test. Studies in female rats did not show impaired fertility. Effects on male fertility have not been determined. Pregnancy (Category C): There are no adequate and well-controlled studies in pregnant women. ISOPTIN crosses the placental barrier and can be detected in umbilical vein blood at delivery. This drug should be used during pregnancy, labor, and delivery, only if clearly needed. Nursing Mothers: ISOPTIN is excreted in human milk, therefore, nursing should be discontinued while verapamil is administered. Pediatric Use: Safety and efficacy of ISOPTIN in children below the age of 18 years have not been established.

ADVERSE REACTIONS: Constipation 8.4%, dizziness 3.5%, nausea 2.7%, hypotension 2.5%, edema 2.1%, headache 1.9%, CHF/pulmonary edema 1.8%, fatigue 1.7%, bradycardia 1.4%, 3° AV block 0.8%, flushing 0.1%, elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1.0% of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain; they are mentioned to alert the physician to a possible relationship: angina pectoris, arthralgia and rash, AV block, blurred vision, cerebrovascular accident, chest pain, claudication, confusion, diarrhea, dry mouth, dyspnea, ecchymosis or bruising, equilibrium disorders, exanthema, gastrointestinal distress, gingival hyperplasia, gynecomastia, hair loss, hyperkeratosis, impotence, increased urination, insomnia, macules, muscle cramps, myocardial infarction, palpitations, paresthesia, psychotic symptoms, purpura (vasculitis), shakiness, somnolence, spotty menstruation, sweating, syncope, urticaria. Treatment of Acute Cardiovascular Adverse Reactions: Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately, e.g., intravenously administered isoproterenol HCl, levarterenol bitartrate, atropine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, inotropic agents (dopamine or dobutamine) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including cardiopulmonary resuscitation.

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

knoll®

BASF Group

©1986, BASF K&F Corporation 2474/11/86 Printed in U.S.A.

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
MAR 25 1987

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℠

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

Rhode Island Medical Journal

March 1987
Volume 70, Number 3

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Jack A. Perkins
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Guy A. Settipane, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

***Edward R. Feller, MD**

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Peter D. T. Clarisse, MD
President

Richard G. Bertini, MD
President-Elect

Milton W. Hamolsky, MD
Secretary

Kenneth E. Liffmann, MD
Treasurer

Herbert Rakatansky, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401-331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

TABLE OF CONTENTS

107 **EDITORIAL**

Catastrophic Coverage A Delusion

Seebert J. Goldowsky, MD

CONTRIBUTIONS

109 **Disseminating Intravascular Coagulation**

Following First Trimester Abortion in Polycythemia Vera

Increased Platelet Count Apparently Contributed to Fatal Outcome

James P. Crowley, MD
Yussef Barcohana, MD
William Q. Sturner, MD

113 **A Five Year Review of Hymenoptera Allergy: 299 Patients**

Refined Venoms Utilizing Only the Antigenic Enzymes in the Venom Are on the Horizon

George K. Boyd, MD
S. G. Chamberlain, RN
B. A. Howard, BSN

121 **Understanding the Smoking Problem and How to Help Patients Stop: Current Status of the Field**

New Behavioral Treatments Prompt Cautious Optimism On Controlling Tobacco Addiction

David B. Abrahms, PhD

127 **Dollars and Sense of Percutaneous Biopsy**

Demonstrates the Cost Effectiveness of the Procedure

Landy P. Paolella, MD
John J. Cronan, MD
Gary S. Dorfman, MD
Alfredo R. Esparza, MD

COVER: *Drawing of the universal symbol for "No Smoking" — a familiar sight within many workplaces and establishments today.*

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml *(1 teaspoonful)* contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg *(warning: may be habit forming)*; alcohol, 3.5 percent, in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

© A.H. Robins Company 1985

EDITORIAL

Catastrophic Coverage A Delusion

As this is written, President Ronald Reagan has just announced his proposal to introduce catastrophic insurance for Medicare recipients. By increasing the Part B premium by $4.92 per month, the new amendments to the Medicare law would assure that no recipient would have to spend more than $2000 out of pocket in any one year. This will apply to a very small segment of Medicare patients. With the vigorous pursuit of DRGs and with the limited scope of the acute nursing care provisions, the real cause of pauperization by illness of the elderly is not addressed. The Catastrophic Health Insurance Plan (CHHP) of Rhode Island has proved to be useful. It is applicable to younger patients, but again meets the needs of very few recipients, often children with such problems as burns and orthopedic disorders.

Simultaneously with the catastrophic Medicare coverage proposals, the Reagan administration recommends increases in the Medicare deductibles and co-insurance. Representative Claude Pepper of Florida, not always a favorite of this writer, has loudly pointed out the irony of this and the snake-oil political cynicism of the new concepts.

The problem lies in the services which Medicare does *not* cover, even with catastrophic coverage. An elderly person requiring long-term care must pay for it himself or herself until his resources have been reduced to $1500. The skilled nursing provisions rarely provide for more than a month or two of care. At present costs of up to $30,000 for a year of nursing home care, very few elderly nursing home residents are not pauperized if they survive long enough.

It is perhaps not fair to portray the administration as totally unmindful of this issue. Doctor Otis R. Bowen, Secretary of DHHS, has stated that financing long-term care is "without a doubt the pre-eminent issue of our time" and has appointed a task force to study the problem and issue recommendations. The leaning, however, seems to be toward leaving it to the "private sector."

Long-term care coverage is not the only deficiency. Elderly persons have expensive eye-care, dental, drug, and sometimes home-care requirements that the federal government will not touch with a special ten-foot pole. Why? Because they are too expensive.

Seebert J. Goldowsky, MD

Rhode Island

ADVERSE DRUG REACTION Reporting Project

SUSPECT A SERIOUS OR UNEXPECTED

ADVERSE DRUG REACTION?

Please Report It.

SUSPECTED ADVERSE REACTION REPORT (For All Drugs and Biologics)

IMPORTANT: SUBMISSION OF A REPORT DOES NOT NECESSARILY CONSTITUTE AN ADMISSION THAT THE DRUG CAUSED THE ADVERSE REACTION

PATIENT INITIALS (Optional)	AGE (Years)	SEX	DATE OF REACTION ONSET
A.D.R.	54	☑ MALE ☐ FEMALE	12 Oct. 1986

DESCRIBE REACTION(S) (Give signs, symptoms, diagnoses, course and lab findings)

JAUNDICE

CHECK ALL APPROPRIATE TO REACTION
- ☐ DIED
- ☑ TREATED WITH Rx DRUG
- ☑ INPATIENT HOSPITALIZATION
- ☐ SEVERE OR PERMANENT DISABILITY
- ☐ EMERGENCY ROOM TREATMENT
- ☐ TREATMENT IN PHYSICIAN OFFICE
- ☐ NONE OF THE ABOVE

SUSPECTED DRUG(S) (Trade Name is preferred. If a generic product, give manufacturer. Indicate Lot No. for vaccines/biologics)

[redacted]

REASON FOR USE OF DRUG(S)	ROUTE	TOTAL DAILY DOSE	DATES OF ADMINISTRATION
HYPERTENSION	P.O.	100mg.	9 Sept.- 12 Oct. '86

OTHER DRUGS TAKEN CONCOMITANTLY (Exclude those used to treat reaction)

None

OTHER RELEVANT HISTORY (e.g. Concomitant Diagnoses, Pregnancy, etc.)

None

PHYSICIAN NAME AND TELEPHONE NUMBER

J. Doe, M.D. 277-2550

Confidential

ALSO REPORTED TO MANUFACTURER ☑ YES ☐ NO

For report forms, guidelines and information contact S. Rosenbaum, PhD, 277-2901

A pilot project of the Rhode Island Department of Health
sponsored by the U.S. Food and Drug Administration

Disseminated Intravascular Coagulation Following First Trimester Abortion in Polycythemia Vera

Increased Platelet Count Apparently Contributed to Fatal Outcome

James P. Crowley, MD
Yussef Barcohana, MD
William Q. Sturner, MD

Polycythemia rubra vera (PRV) is rarely encountered in pregnancy since it is generally a disease of later life.[1,2] In 1983 Ferguson and co-workers[3] reported the case of a young woman who had negotiated two pregnancies without difficulty. In this report they reviewed the literature and found that a total of 13 pregnancies had been reported in 8 women. Although there was a higher than expected incidence of hypertension, and also some evidence of perinatal mortality, there was no maternal mortality. Fatalities following first trimester curettage termination of pregnancy are also rare in normal women[4,5] and not previously reported in PRV.

James P. Crowley, MD, is Associate Professor at Brown University Department of Medicine. He is recipient of a Transfusion Medicine Academic Award from the National Heart, Lung and Blood Institute (KO7 HL01259-01A1).

Yussef Barcohana, MD, is Chief, Department of Anesthesiology, Women and Infants Hospital, and Associate Clinical Professor of Obstetrics & Gynecology (Anesthesiology) at Brown University.

William Q. Sturner, MD, is Chief Medical Examiner, State of Rhode Island, Medical Examiner's Office.

The opinions or statements of the authors are not to be construed as representing or reflecting official policy of the Rhode Island Department of Health or the State of Rhode Island.

In the present study, we describe the first case of a patient with PRV with a fatal outcome during pregnancy. A severe disseminated intravascular coagulation (DIC) accompanied by multiple thromboemboli at various sites was the cause of death. The catastrophe appeared to be triggered by a first trimester therapeutic abortion by suction curettage.

Case Report

A 25-year-old Portugese-speaking woman missed two menstrual periods and consulted a physician, who diagnosed a pregnancy estimated to be in the fifth or sixth week of gestation. The patient indicated that she desired a termination. Her past medical history was unremarkable, but blood counts obtained two months earlier showed a packed cell volume of 59 v per cent. Her hemoglobin was now 16.6 g/dl, with a hematocrit of 49.5 v per cent, white count 13,000/ml, and platelet count 1.5 million/ml.[3] The mean corpuscular volume (MCV) was 75 μ.[3] Physical examination revealed a gravid abdomen and a palpably enlarged spleen. A bone marrow aspirate and biopsy (Figure 1) showed severe erythroid and myeloid hyperplasia and was interpreted as consistent with polycythemia vera. The leukocyte alkaline phosphatase (LAP) score was 120 (elevated) and erythropoietin levels were zero. The patient was treated with dipyridamole 50 mg three times daily and aspirin 5 grains daily for her thrombocytosis. A red-cell mass study was not performed because of some uncertainty that the patient would follow through with her decision to terminate the pregnancy. The patient was seen again one month later.

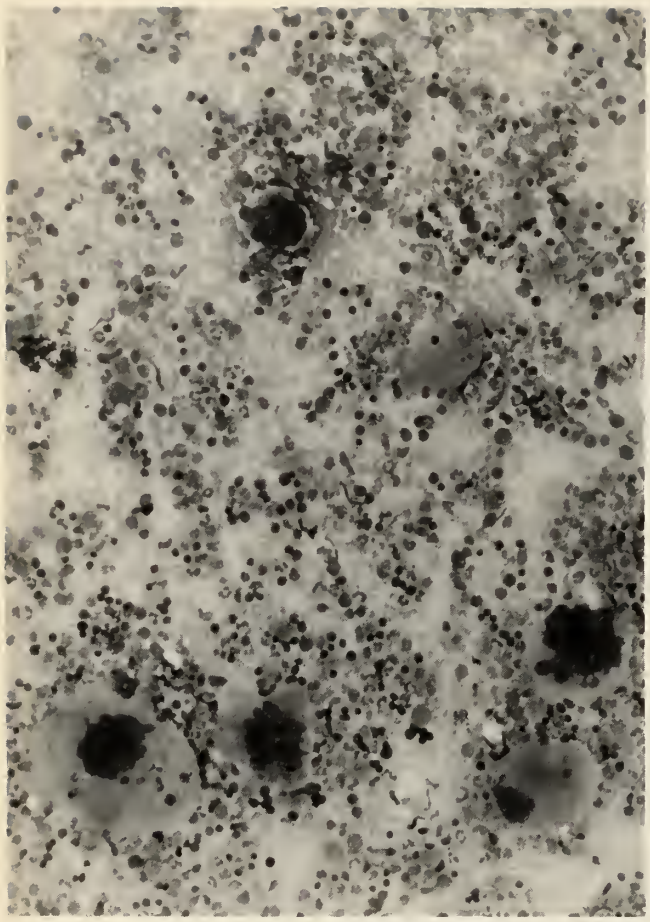


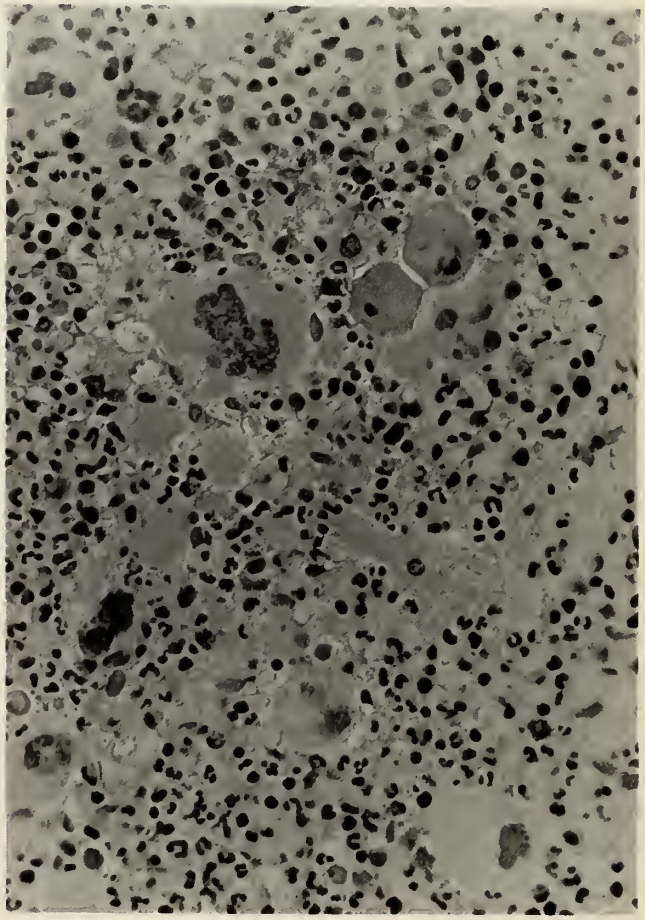
Figure 1: Bone marrow aspirate obtained from patient one month before fatal DIC.

A: Wright-Giemsa stained marrow showing marked myeloid and megakaryocyte hyperplasia (500x).

Premedication was given at 10:50 am on the morning of the termination procedure. General anesthesia was administered at 10:54 am, and suction curettage was done at 11:00 am. The anesthesia was sodium pentothal and nitrous oxide by mask. Immediately after the procedure she became cyanotic and her heart stopped. The anesthesiologist intubated and oxygenated the patient. An emergency computed tomography (CT) scan of the brain was normal, and a lung scan showed extensive pulmonary emboli. Partial thromboplastin time (PTT) and prothrombin values (PT) were extremely prolonged (PTT 154 seconds, PT >100 seconds), and her fibrinogen was not measurable. Her platelet count had fallen to 800,000/ml.[3] Fibrin degradation products were increased (>1:80) in the serum and plasma. Arterial blood gases showed hypoxia and respiratory alkalosis despite intubation. Heparin and plasma were administered with an obvious decrease in oozing at venipuncture sites. Her fibrinogen was 130 mg/dl by 8 hours following the arrest, but her platelet count fell to 320,000/ml.[3] Despite intensive care, her pulmonary problem was intractable, and she died a week later. Postmortem findings included pulmonary thromboemboli with infarction, left iliac vein thrombosis, and segmental thrombosis of the sagitital sinus of the brain. The liver and spleen were enlarged and showed evidence of extramedullary hematopoiesis.

Figure 1: Bone marrow aspirate obtained from patient one month before fatal DIC.

B: H and E section of marrow showing dysmyelopoietic megakaryocytes (500x).



Discussion

This woman is the first pregnant polycythemia vera patient with a fatal outcome reported in the literature.[3] Because she was pregnant, ^{51}Cr blood values were not performed, but there seems little

doubt given the other findings that she had polycythemia vera. Her hematocrit was abnormally high, and the splenomegaly, increased LAP, low erythropoietin and appearance of the marrow all strongly supported the diagnosis. The low MCV is consistent with iron deficiency, and the patient may have had occult bleeding in the past.

Polycythemia rubra vera (PRV) is a disease which is usually diagnosed after the sixth decade.[1, 2, 6] It is not surprising therefore, that only a small number of pregnancies have been described. Ferguson et al[3] after reviewing the literature of PRV and pregnancy in 1983 concluded that the initial hematologic values were not helpful in predicting outcome. However, live births resulted from all pregnancies in women with initial red blood count of 5 million/ml respectively. Somewhat unexpectantly, post-partum hemorrhage or thrombosis did not occur in any of these pregnant patients. A significant fall in hematocrit and platelet count occurred during pregnancy, which was ascribed to hemodilution. The hemodilutional effect of late pregnancy may have reduced the thrombotic tendency by lowering whole blood viscosity. Previous studies document well the danger of hematocrits over 55 v per cent and their association with a high post-operative morbidity and mortality in PRV which is not associated with pregnancy.[1, 2] The present patient had a hematocrit less than 50 v per cent at the time of delivery. Because of the "minor" nature of the procedure, phlebotomy was not recommended.

Severe hypofibrinogenemia is not seen in uncomplicated polycythemia vera, although reports of moderate reduction of fibrinogen have appeared.[1] The very low fibrinogen observed in the present case was thus consistent with a severe DIC.[7] Goss in 1978[5] first reported DIC as a complication in first trimester curettage. A 25-year-old woman was given a general anesthetic after an intravenous oxytoxin drip. No problems were immediately evident, but following curettage substantial blood loss occurred from the uterus. Coagulation studies were diagnostic of DIC. The patient survived this episode with transfusion therapy.

A 32-year-old woman was reported[8] who developed prolonged cardiovascular and pulmonary collapse following the evacuation of an 18-week missed abortion. The sudden catastrophe and severe DIC[7] strongly suggested that an amniotic fluid embolism had occurred. A negative Papanicolaou (Pap) smear of the sputum did not negate the clinical diagnosis, since only a small

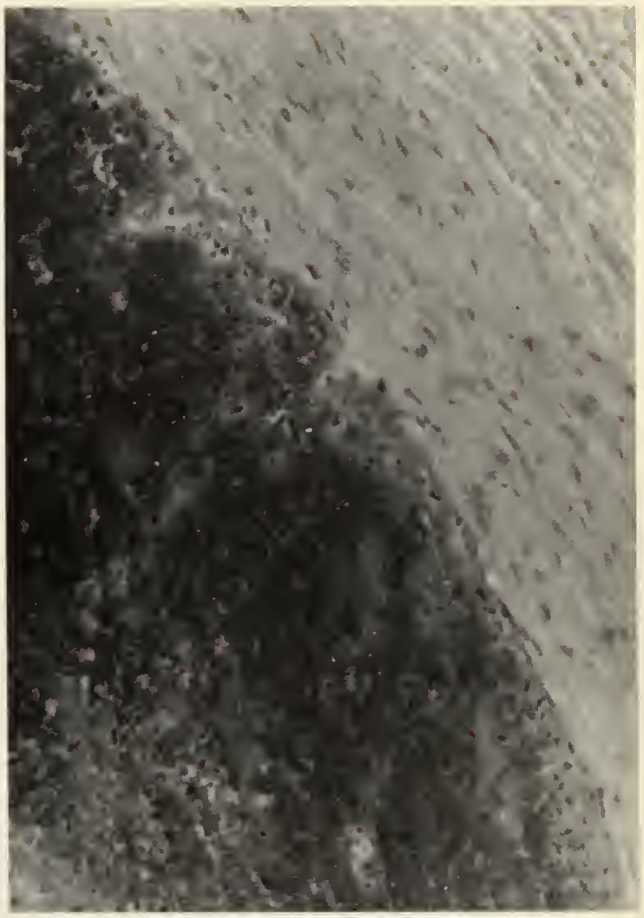


Figure 2: Detail of organizing thrombus in large pulmonary vein.

volume of fluid must enter the circulation in a first trimester suction curettage. Although amniotic fluid embolism is a plausible explanation of the DIC in this patient, an alternative cause would be the cardiac arrest. Cardiac arrest can cause DIC with acute depletion of fibrinogen and platelets. The cardiac arrest may have been precipitated by a pulmonary embolism from the left iliac vein thrombosis. The thrombotic problems in the present case were seemingly unaffected by the aspirin and dipyridamole prescribed in the preceding month.

This patient's platelet count was higher than any of the pregnant patients previously reported in the literature.[3] Moreover, the platelet count noted initially to be 1.2 million/ml was 800,000/ml after the arrest, and 146,000/ml two days later. The high platelet count may have produced or exacerbated a hypercoagulable state.[9] Lowering the platelets with drug therapy was considered. However, the use of alkylating agents to lower

the platelet count of pregnant women in the first trimester is usually avoided, since it may precipitate an abortion. Moreover, these drugs may also be teratogenic. On this patient's first visit, a firm decision for abortion had not been made.

While the experience of a single unfortunate individual cannot be the basis for any firm conclusions, a vigorous attempt to lower the platelet count with a rapid acting agent such as hydroxyurea should be considered in future cases.

Summary

A patient with polycythemia vera with a fatal outcome during pregnancy is described. A review of the literature disclosed no other instance of such an unfortunate event. Death immediately followed a first trimester curettage termination of pregnancy. The patient's platelet count was higher than that of the pregnant patients reported in the literature. The increased numbers of abnormal platelets may have exerted a potentiating effect on thrombogenic factors released during the abortion.

Acknowledgements

The authors thank Drs Curtis Harris, Charles Foote and Phillip O'Dowd for helpful information concerning the patient's hospital care. Ms Judy Morris provided expert secretarial assistance and Mrs Jaclyn Metzger photographed the marrow sections.

References

1. Wasserman LR, Gilbert SH: Surgery in Polycythemia Vera. N Engl J Med, 269(23):1226-1230, 1963.
2. Chievitz E, Thiede T: Complications and Causes of Death in Polycythemia Vera. Acta Med Scand, 172:513-523, 1962.
3. Ferguson JE, Ueland K, Aronson WJ: Polycythemia Rubra Vera and Pregnancy, Obstet Gynecol, 62(3):16S-20S, 1983.
4. Cates W, Boyd C, Halvorson-Boyd G, et al: Death from Amniotic Fluid Embolism and Disseminated Intravascular Coagulation after a Curettage Abortion. Am J Obstet Gynecol, 141:346-348, 1981.
5. Goss AS: Disseminated Intravascular Coagulation Syndrome After Vacuum Curettement for First Trimester Abortion. South Med J, 71(8):967-969, 1978.
6. Silverstein MN, Lanner AP: Polycythemia Vera. Mayo Clin Proc, 46:751-755, 1971.
7. Crowley JP: The Diagnosis and Treatment of Thrombocytopenia and Intravascular Coagulation in Late Pregnancy. RI Med J, 66:331, 1983.
8. Stromme WB, Fromke VL: Amniotic Fluid Embolism and Disseminated Intravascular Coagulation after Evacuation of Missed Abortion. Obstet Gynecol, 52(1):76S-80S, 1978.
9. Schafer AI: The Hypercoagulable States. Ann Intern Med, 102:814-828, 1985.

593 Eddy Street
Providence, RI 02902

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY . . . . ANYWHERE

PLUS insurance for . . . .
tax audit
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

A Five Year Review of Hymenoptera Allergy: 299 Patients

Refined Venoms Utilizing Only the Antigenic Enzymes in the Venom Are on the Horizon

George K. Boyd, MD
S. G. Chamberlain, RN
B. A. Howard, BSN

The efficacy of purified venom therapy for Hymenoptera allergy has been verified by the early reports of Valentine, Sobotka et al from Johns Hopkins University. They were the first to successfully desensitize a beekeeper's son with honey bee venom in 1971.[1] This early report was rapidly followed by many others utilizing wasp and vespid venoms.[2-4]

Whole body extract (WBE) for bee sting protection was widely used for many decades. However, it is no longer recommended for venom anaphylaxis and was withdrawn from commercial use in January 1986 by the Food and Drug Administration (FDA).

This review represents our experience in evaluating 299 patients referred to our office and the allergy clinic at the Rhode Island Hospital for apparent anaphylactic reactions to the stinging insects. It includes a demographic overview and current recommendations for treatment. All patients were seen between January 1980 and December 1984 and were referred from the greater Providence area and surrounding Southeastern Massachusetts.

George K. Boyd, MD, is a Pediatric Allergist in Providence.

S. G. Chamberlain, RN, is employed by Dr. Boyd.

B. A. Howard, BSN, is employed by the Allergy Division of R. I. Hospital.

The stinging insects are classified under the major biologic order of the Hymenoptera, meaning membranous winged. The four insects, commonly named yellow jackets, hornets, wasps and honey bees are shown in their basic family subdivisions in Chart 1. The relative similarities between the yellow jackets and hornets are readily apparent, while the wasps and honey bees are seen in quite separate family "lines."

Studies from 1970, 1971, and 1972 on the incidence of stinging insect allergic reactions in a boy and girl scout population in Rhode Island showed a frequency of between 3.5 and 8/1000.[5, 6, 12] More recent studies (1981) in a Baltimore plant with adults have shown a higher rate of 4 per cent with *reported* bee sting reactions. Skin tests were then performed on this group with 20 per cent showing positive skin test titers.[7]

The Criteria for Patient Selection

Early in the history of commercially available venoms, many allergists felt that almost any type of reaction to a stinging insect should be treated with active venom therapy. We chose a much more conservative approach due to the high cost of obtaining the raw material for venom treatment and the long period of time required for venom therapy. We followed most of the guidelines and recommendations initially made by the Johns Hopkins group and the modified Yocum, Johnstone, and Condemi[8] classification of anaphylaxis as a basis for early selection of potential candidates for venom immunotherapy:

GRADE 1: Any local reaction regardless of severity (eg swelling of an entire limb, with erythema, but not becoming general).

GRADE 2: Generalized cutaneous reaction, primarily urticaria with or without angioedema but no respiratory signs or vascular collapse.
GRADE 3: Any respiratory signs of dyspnea, glottic edema, and wheezing.
GRADE 4: Total vasomotor collapse and shock, possible cardiac arrest.

(Grades 3 and 4 may or may not be accompanied by urticaria and angioedema. Gastrointestinal symptoms, eg vomiting, and diarrhea, would be included in the Grade 3 classification.)

Valentine, Sobotka and Lichtenstein's group at Johns Hopkins prefer to use the terms: non-life threatening for Grades 1 and 2, and life threatening reactions for Grades 3 and 4. These terms are more precise and reduce the grading criteria from 4 to 2 categories.

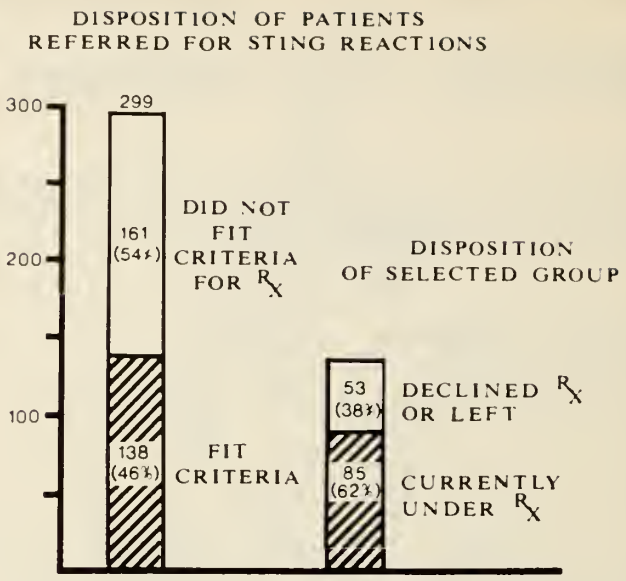
Our basic recommendation was to advise skin testing titrations and therapy to most adults with Grade 3 and 4 reactions. We did not strongly oppose testing and treating Grade 2 reactions (cutaneous) if the patient were at all concerned about the likelihood of future stings, and had reservations about their ability to use or carry an epinephrine kit. We did not recommend venom therapy for children under 12 with either Grade 1 or 2 cutaneous reactions. Completed studies from Johns Hopkins with a controlled series of children treated and untreated for over two years showed quite dramatically that children have only a 10 per cent chance of even repeating a Grade 2 experience, and overwhelmingly show no reaction at all, whether treated with venom therapy or not![9] Serum-specific IgE levels have also been shown to decrease over time, again even in those children not receiving any immunotherapy to the original specific venom sensitivity.[10]

Characteristics of the 299 Patients Evaluated

Figure 1 bar graphs show the initial separation of the originally referred patients into those who fit the critera for immunotherapy and those who did not. In addition, it illustrates the final disposition of the 138 patients selected after a number left the treatment program or declined venom therapy.

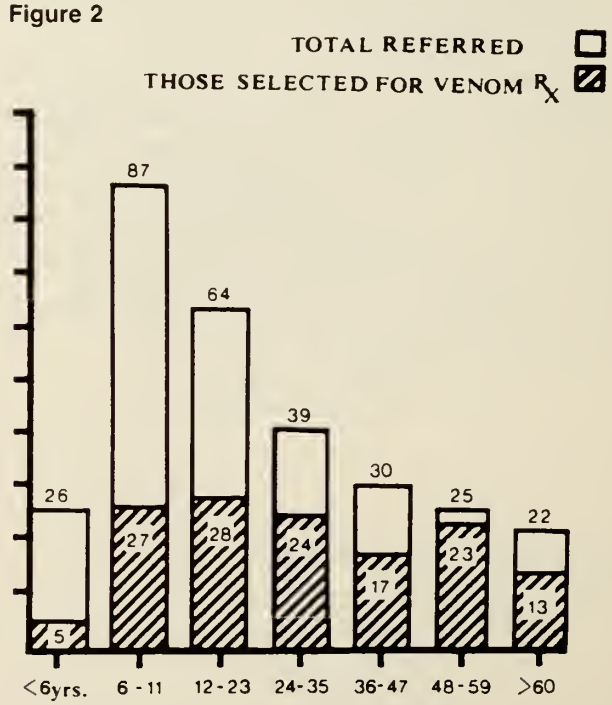
The Figure 2 bar graph shows the age distribution of the original 299 patients referred to us for insect sting reactions for possible venom therapy (clear bars). The shaded bars in each age grouping represent the number from each age bracket who fulfilled our criteria for Grade 3 or 4 reactions and therefore were candidates for specific immunotherapy (138 patients).

Figure 1



The age range of the 299 original patients was 2 to 73 years with a mean age of 24.1 years. The age range of the selected group for active therapy was 4 to 73 years with a mean age of 30.8 years. The shift of the age mean of the initial set to an older mean in the final selected treatment set is readily apparent in Figure 2. When strict criteria for selection to active venom therapy was observed, a greater proportion of children under 12 were eliminated from treatment considerations.

Figure 2



AGE DISTRIBUTION OF ALL 299 PATIENTS

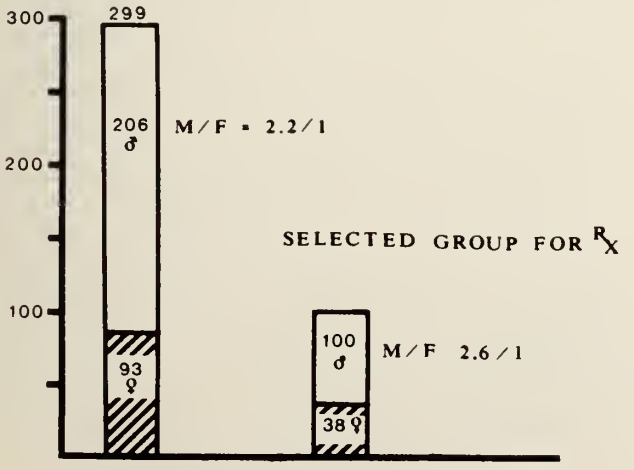
In Figure 3 the sex ratios between the initially referred 299 patients and the ratios found in the finally selected 138 patients are compared. The preponderance of males is apparent in both, but the ratio increases even more for males in the treatment selected number, 2.2/1 to 2.6/1!

The monthly frequency distribution of stings as reported by 266 patients is demonstrated in Figure 4. There is no question that August is the most likely month in this area in which to encounter a bee sting. There is almost a bell-shaped distribution between June and October, while April and November provide only one percent of the total reports. The frequency of positive skins test titers at a dilution of 0.1/μg/ml or less in 269 positive tests is shown in Figure 5. In the geographic area centered in Rhode Island, the vespid group (yellow jackets and hornets) are the most frequent sensitivities found (81 per cent). The wasps represent 17 per cent of all positive tests, and the honey bee is a distinct minority (two per cent) of all skin test reactions found.

Original estimates of efficacy in preventing subsequent anaphylactic reactions by specific venom therapy were reported approaching 95 per cent[10] at maintenance dosages of 100 μg of venom given at monthly intervals. Recent data place this figure closer to 98 per cent and Reisman of Buffalo has a series of patients on maintenance levels of 50 μg reportedly reaching efficacy levels of 80 per cent prevention of sting anaphylaxis.[15]

We encountered one patient with a failure to a subsequent wasp sting after reaching maintenance levels of 100 μg for over six months. He was then slowly raised to 200 μg as a wasp maintenance level of venom therapy. Second and third stings were encountered without incident some months later. Between the time of his reaction sting (following six months of standard therapy) and the time required to increase his maintenance dose to 200 μg (six months), he demonstrated serum IgE sensitizing wasp antibody reduction and specific IgG protective wasp antibody increase.

Figure 3



SEX DISTRIBUTION OF PATIENTS REFERRED FOR STING REACTION

Figure 4

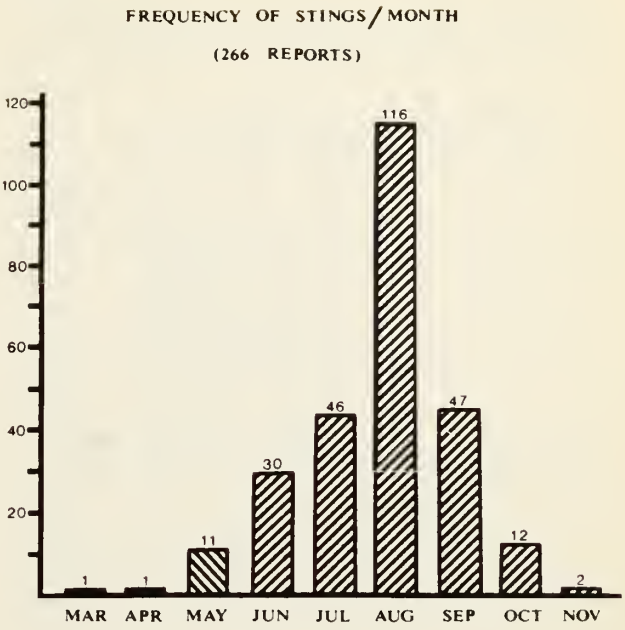
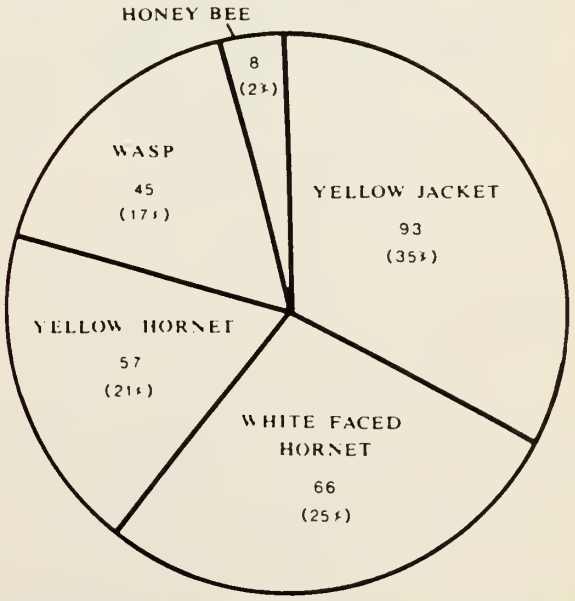


Figure 5



FREQUENCY OF POSITIVE SKIN TITERS ≤ 1ug/ml

Of the treated group, 20 were restung with all but one (same patient as above) experiencing no reaction or only a modified Grade 1 local reaction. This represents an efficacy rate of 95 per cent in our known repeat stings.

To summarize our experience in the greater Providence area and Southeastern Massachusetts based on our evaluations and follow-up of 299 originally referred patients for bee sting allergy, the following composite can be drawn: 1. The most likely bee sting reaction candidate is a male. 2. His mean age is approximately 30.8 years of age. 3. He will most likely be stung in the month of August. 4. Overwhelming, he will be stung by a member of the Vespid Hymenoptera, with the yellow jacket (Vespula) the most likely genus. 5. The least likely genus to cause a severe reaction in this area appears to be the honey bee (Apis). (It is of more than passing interest that the one patient on honey bee venom therapy from our private practice group is a bee keeper, who is now stung almost weekly without incident.)

It is of interest that a personal history of major allergy was found in only 21 of the 138 selected treatment group (15 per cent). This is well within an accepted range for the normal occurrence of allergy in the general population, and agrees with previous studies[11, 12] demonstrating an expected normal atopic frequency in a bee sting sensitive population.

Conclusions and Recommendations

The final chapter on Hymenoptera anaphylaxis is far from finished. More refined venoms utilizing only the antigenic enzymes in the venom are on the horizon. Reisman et al[13, 14] have made some exciting observations showing a considerable cross-antigenicity of all the Vespids. The likelihood of treating with only one of the vespids (eg yellow jacket) and protecting against all hornets as well, may eventually be a generally acceptable option for all vespid sensitive patients.

The duration of therapy is also under intense review. A recent report at the annual meeting of the American Academy of Allergy and Immunology (AAAI) in New Orleans (March 1986) by Golden et al[15] notes continuing protection a year (and longer) after the cessation of active immunotherapy. This apparently occurs in spite of very low circulating specific IgG protective levels.

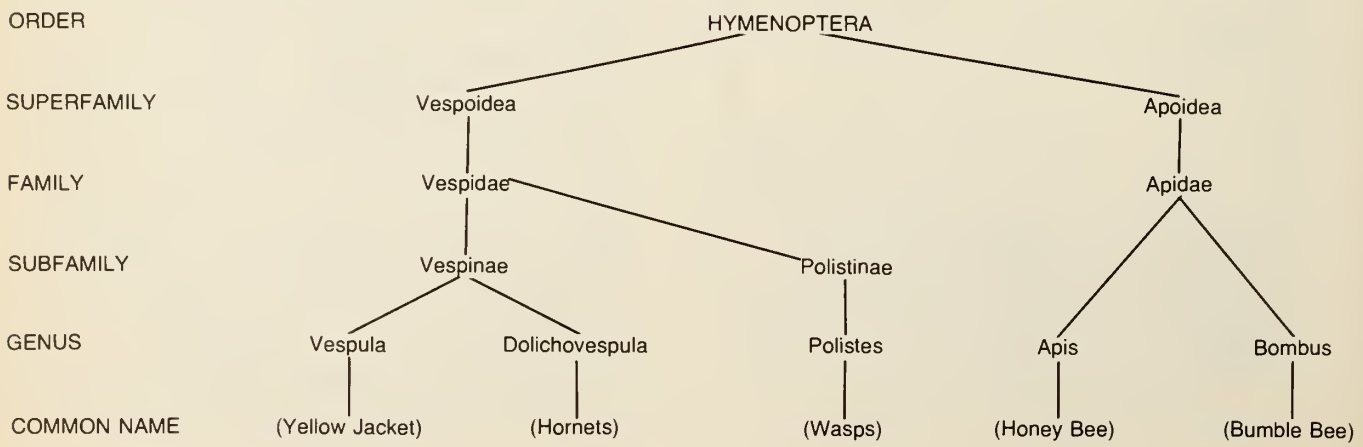
We propose the following guidelines for venom immunotherapy in basic agreement with recently published guidelines by the insect committee of AAAI:[16]

1. Children under 12 years of age are a very special subset of insect sting reactors. Only 10 per cent of those with a Grade 2 reaction will be expected to repeat a similar reaction, and 90 per cent will experience a less severe reaction or none at all if restung. We do not recommend testing or treating children with this non-life threatening reaction.

2. Adults experiencing a Grade 2 (cutaneous) reaction are also unlikely to increase the severity of reaction with a subsequent sting. In fact, Reisman[15] believes that cutaneous reactions in the adult have outcomes similar to those of children under 12. Our policy has been not to test or treat these adults.

3. Adults and children with a documented history of a Grade 3 reaction should be tested and titrated for specific hymenoptera venoms, and treatment should be recommended.

Chart 1



4. In adults and children with a history of Grade 4 reactions (vasomotor collapse), therapy is absolutely indicated when accompanied by corroborating skin test and serum venom titers.

5. All patients with a Grade 2, 3, or 4 reaction should always have an emergency epinephrine kit available.

6. The expected systemic reaction prevention rate for venom treated patients now approaches 98 per cent.

7. The eventual discontinuation of all immunotherapy after 4 or 5 years of therapy will probably be possible in the future for a large number of patients.

References

[1] Lichtenstein LM, Valentine MD, Sobotka AK: A case for venom treatment in anaphylactic sensitivity to hymenoptera sting. N Eng J Med 290:1223, 1974.

[2] Hunt KJ, Valentine MD, Sobotka AK, Benton AW, Amodia FJ, Lichtenstein LM: A controlled trial of immunotherapy in insect hypersensitivity. N Eng J Med 299:157, 1978.

[3] Reisman RE, Dvorin DJ, Randolph CC, Georgitis JW: Stinging insect allergy: Natural history and modification with venom immunotherapy. J Allergy Clin Immunol 75:735, 1985.

[4] Golden DBK, Kagey-Sobotka A, Valentine MD, Lichtenstein LM: Dose dependence of hymenoptera venom immunotherapy. J Allergy Clin Immunol 67:370, 1981.

[5] Settipane GA, Boyd GK: Prevalence of bee sting allergy in 4992 boy scouts. ACTA Allergologica 25:286, 1970.

[6] Abrishami MA, Boyd GK, Settipane GA: Prevalence of bee sting allergy in 2010 girl scouts. ACTA Allergologica 26:117, 1971.

[7] Golden DBK, Valentine MD, Kagey-Sobotka A, Lichtenstein LM: Prevalence of Hymenoptera venom allergy. J Allergy Clin Immunol 69 (suppl):124, 1982.

[8] Yocum MW, Johnstone DE, Condemi JJ: Leukocyte histamine release in hymenoptera-allergic patients. J Allergy Clin Immunol 52:265, 1973.

[9] Schuberth KC, Graft DF, Kwiterovich KA, Kagey-Sobotka, Szklom M, Lichtenstein LM, Valentine MD: Discontinuation of venom immunotherapy in children. J Allergy Clin Immunol 73:189, 1984.

[10] Golden DBK, Johnson K, Addison BI, Valentine MD, Kagey-Sobotka A, Marsh DG, Lichtenstein LM: Evolution of hymenoptera venom allergy. J Allergy Clin Immunol 73:189, 1984.

[11] Settipane GA, Klein DE, Boyd GK: Relationship of atopy and anaphylactic sensitization: a bee sting allergy model. Clin Allergy 8:259, 1978.

[12] Settipane GA, Newstead GJ, Boyd GK: Relationship of hymenoptera allergy in an atopic and normal population. J Allergy Clin Immunol 50:146, 1972.

[13] Reisman RE, Mueller UR, Wypych J, Elliott W, Arbesman CE: Comparison of the allergenicity and antigenicity of yellow jacket and hornet venoms. J Allergy Clin Immunol 69:268, 1982.

[14] Reisman RE, Wypych JI, Mueller UR, Grant JA: Comparison of the allergenicity and antigenicity of polistes venom and other vespid venoms. J Allergy Clin Immunol 70:281, 1982.

[15] Schwartz HJ, Reisman RE, Valentine MD, Yunginger JW, Golden DBK, Müller V: Workshop: insect allergy. AAAI Annual Meeting, New Orleans, LA: March 22, 1986.

[16] Golden DBK, Schwartz HJ for the Committee on Insects: AAAI: Guidelines for venom immunotherapy. J Allergy Clin Immunol 77:727, 1986.

HOME NURSING CARE

Private Duty Nursing

* REGISTERED NURSES
* LICENSED PRACTICAL NURSES
* NURSE AIDES
* HOMEMAKERS
* HOME HEALTH AIDES

When Home Care Is Needed

Please Call . . .

CATHLEEN NAUGHTON ASSOCIATES

Employes Bonded and Insured

cna

(401) 751-9660

Available 7 days a week
24 hours a day.

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

There are three ways to bill

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj	CURRENT BALANCE
		BALANCE FORWARD →				60.
8/30/85	James	Bal. Forward				60.
9/5/85	" "	O.V	40.	Billed 9/5/85		100.
9/30/85		Medicare pmt/adj.		45.	-8.	47.
10/10/85		patient pmt.		-7.		40.
10/25/85		Medicare pmt/adj.		-28.	-5.	7.
11/10/85		Pt pmt.		-7.		-0-
11/20/85	James	Int. O.V	40.	Billed 11/21/85		40.
12/5/85	James	Surgery	800.	Billed 12/20/85		840.
1/5/86		Medicare pmt/adj		-280.	-5.	555.
1/17/86		Court. adj.			-3.	552.
2/2/86		Medicare pmt/adj		440.	250.	114.

PLEASE PAY AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86 DATE 2/21/8
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

our patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient year-to-date payment totals.

Words are *printed*. You're not judged by someone else's scribbles.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

STATEMENT

FED I.D. #00-0000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	L O	DESCRIPTION	CHARGES PAYMENTS ADJ. PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT						
	YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS		PATIENT	INSURANCE
.00	4.00	.00	.00	.00	NEW BALANCE	4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT" NEW BALANCE" SHOWN.

02/21/86	.00	12090	
STATEMENT DATE	PATIENT PAY Y.T.D.	ACCOUNT NUMBER	LOCATION CODES: 1 OFFICE, 2 HOSPITAL IN PATIENT, 3 HOSPITAL OUT PATIENT, 4 OTHER, 5 OTHER, 6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A.

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

A WORD TO THE WHYS

WHY AMA? AMA-sponsored Group Disability insurance is designed to replace a substantial portion of your income should you be unable to practice due to sickness or accident. Unlike many policies, AMA-sponsored Disability Insurance provides benefits if you are unable to perform *your* occupation in *your* medical specialty. Providing you with benefits you can't afford to be without: it's one more good reason why you should be a part of the AMA.

WHY AMA? Now, for the first time there's a forum for hospital medical staffs to meet nationally to discuss common problems and changes in physician-hospital relationships. The Hospital Medical Staff Section was recently created by the AMA to provide leadership in ensuring quality patient care during this period of massive hospital restructuring. It's one more good reason why you should be a part of the AMA.

WHY AMA? Commitment to maintaining high quality at all levels of medical education is one of the AMA's proudest traditions. The AMA creates policy for medical education, participates in accreditation activities, and supplies the public with information on medical education issues. Proven dedication to high standards in medical education: it's one more good reason why you should be a part of the AMA.

To Join, Contact your county or state medical society or write: Division of Membership, AMA, 535 North Dearborn Street, Chicago, Illinois 60610 or call collect, (312) 751-6196.

AMA
AMERICAN MEDICAL ASSOCIATION

Understanding the Smoking Problem and How To Help Patients Stop: Current Status of the Field

New Behavioral Treatments Prompt Cautious Optimism On Controlling Tobacco Addiction

David B. Abrams, PhD

This paper highlights recent findings on smoking and health with emphasis on evaluating and treating adult smokers and reviews the current status of both brief and comprehensive smoking cessation programs. Specific recommendations are made regarding implementation of a step-care approach to assist patients to stop smoking, identifying tactics for use in physicians' practices, and criteria to evaluate patients and the quality of smoking cessation programs.

The Health Hazards of Smoking

DSM-III[1] defines tobacco dependence as: continual use of tobacco for at least one month with either a) unsuccessful attempts to stop or reduce intake on a permanent basis, b) development of a withdrawal syndrome, or c) the presence of a serious physical disorder that the individual knows is exacerbated by tobacco use.[1] The most common form of tobacco use is cigarette smoking, but use of chewing tobacco is growing at an alarming rate.[2]

David B. Abrams, PhD, is a Clinical Psychologist, Assistant Professor of Psychiatry and Human Behavior, Brown University, and the coordinator of the Center for Health Promotion at The Miriam Hospital, which provides lifestyle modification services.

From The Brown University Program in Medicine and The Center for Health Promotion, The Miriam Hospital.

In order better to treat patients, it is important to know who is at high risk for illness and what factors make cigarettes so appealing that people cannot give up the habit even if they want to. Smoking remains the leading preventable cause of cancer and cardiovascular disease (CVD). In 1980, cancer accounted for 412,000 deaths, of which a third were attributed to smoking, primarily lung cancer.[3] While it is common knowledge that smoking causes cancer, the general population is less aware of the role smoking plays in CVD and its multiplicative interactions with other CVD risk factors such as hypertension. It is estimated that 24 million people (10 per cent of all persons now living) will die prematurely of CVD attributable to smoking.[4] The unnecessary costs of smoking exceeded $60 billion in 1982.

In 1955, 54 per cent of men but only 24 per cent of women smoked. By 1983 both men and women were smoking at roughly the same rate (28-31 per cent). In 1950 less than five women per 1,000 per year died of lung cancer, whereas 18 died of breast cancer. In 1986, the American Cancer Society reported that lung cancer had overtaken breast cancer as the leading cause of death by cancer in women and the rate of both types of cancer will exceed 35 deaths per 1,000. Women who take oral contraceptives and pregnant women should not smoke. Babies born to smokers have an increased incidence of respiratory problems and birth defects, and have lower birth weights, as compared to the children of non-smokers. All smokers have certainly come a long way — tobacco does not discriminate on the basis of sex, age, or ethnicity with respect to its devastating medical sequelae!

Women may be biologically more sensitive to the effects of nicotine. Nicotine suppresses thyroid functions, and this effect could persist for several weeks after quitting. Thus, withdrawal symptoms, including fatigue, irritability, and depression, may last for a significant period after quitting and make abstinence difficult to maintain.[5] Women over age 40 find it especially difficult to quit smoking. They may use cigarettes for regulation of emotions (eg, depression, anger). Young working women are particularly susceptible to cigarette advertising that stresses ambition, liberation, and glamour. They have been smoking at increasing rates over the past five years.

The bio-behavioral properties of nicotine make it an ideal drug to modulate moods, alleviate fatigue, and stress.[2, 6] Nicotine stimulates beta-endorphin and vasopression. Thus it reduces pain, increases stress tolerance, and improves memory, concentration, and speed of information processing. Some individuals are therefore *psychologically* dependent on the stress-dampening effects of smoking. They may need more extended psychotherapeutic counseling to help them to cope with the anxieties of everyday living. Smoking can also be used to mask social anxiety, or to modulate interpersonal anger or frustration. This is in addition to the obvious pharmacological addiction.

Several studies show that smokers alter their smoking behavior when they switch to low-yield cigarettes. This compensation may lead to an increased uptake of dangerous gas constituents. Therefore it is unlikely that a "safe cigarette" can be developed. Evidence is also mounting against the dangers of second-hand smoke. A recent study[7] reported that non-smokers exposed to cigarettes have significantly higher cancer risks. The workplace is a prime area where restrictive smoking policies can be implemented, including the physician's office and the hospital. Cigarette smoke is a major occupational hazard.

Less than 18 per cent of physicians now smoke. It is important for them to portray the appropriate role models for the public. If possible, physicians and other health care professionals should not smoke in public or while on duty. Finally, there are concerns about the excessive smoking rates in blue-collar workers, among blacks, and in lower educational and SES levels. It is estimated that over 45 per cent of the adults in these sociodemographic groups are still smoking, in contrast to less than 30 per cent of professionals. Smoking is a major correlate of chronic disease. Its rise among women and its persistence in lower SES groups is cause for national concern.

Treatment Strategies

Understanding the unique functions that smoking serves for the patient (and the specific bio-behavioral effects and the types of withdrawal reactions that could precipitate a return to smoking) are critical to treatment planning. These factors can serve as the basis for developing realistic long-term treatment plans.

It is important to note that a) many smokers quit on their own or with low-cost self-help materials, b) knowledge about the health hazards of smoking may increase motivation, but is usually insufficient to result in quitting, and c) many smokers who quit report making anywhere from two to four *unsuccessful* attempts before they succeed. Thus any attempt to quit should be looked upon as a positive learning experience rather than as a "failure" resulting in guilt, avoidance, and hesitation about trying again. Both physicians and their patients must guard against becoming frustrated, feeling helpless, and tending to "give up" on the idea of achieving abstinence. Helping patients quit smoking should be approached in a step-wise fashion, and, if necessary, over several years. While physicians need not provide all the time-consuming treatment, they are in a unique position to play a critical role in motivating the smoker to quit.

There are four major patient characteristics that are useful for evaluation. These are: a) motivation or readiness to change; b) degree of biological addiction; c) degree of psychological dependence; and d) past history of serious attempts to quit.

An individual must be truly ready to take action, and not simply be responding to the pressure of others. DiClemente and Prochaska[8] have identified five critical phases in the change process, including immotive, contemplative, action, maintenance, and termination. Immotive individuals have made an informed quality-of-life decision to remain smokers, and there is little anyone can say or do to motivate them. Few smokers actually fall into the immotive category, although on the surface those of us who try to get smokers to quit might erroneously conclude that most smokers are immotive! Contemplators can generally be moved to action by providing them with information so that the "cons" of smoking begin to outweigh the "pros." Factors that can move an individual from contemplation to action are pressure from family, serious talks

with physicians, follow-up visits or telephone calls to show that the physician "means business," educational materials, and other social pressures such as restrictive smoking policies and smoking-related illnesses in immediate family members. Actually, very few physicians (less than 30 per cent) currently have a serious 10 minute "heart to heart" talk with their patients who smoke until a serious medical problem develops. If all physicians counseled their patients routinely on the dangers of smoking, powerfully and assertively asked their patients to quit, and then followed up with specific suggestions about programs, a tremendous public health impact could result.[2] Persistent follow-up with requests to schedule visits in the future in order to continue to help the struggling patient has also been shown to be very effective.

When the patient is ready to take action, there are four major options for quitting: a) doing it on one's own or with low-cost self-help materials from voluntary agencies; b) brief, minimal interventions such as in the physician's office, or using hypnosis or acupuncture; c) comprehensive quit-smoking programs based on behavior modification principles and usually associated with hospitals, medical schools, or psychology departments, and d) commercial programs. Research shows that nicotine gum should be used only with (c) above and not in isolation at this time.[2]

Upon assuming that an individual is ready for action, one should assess his/her status on the dimensions of biological addiction, psychological dependence, and history of previous attempts to quit. The general rule of thumb is that smokers should receive a comprehensive treatment program if they a) are biologically addicted smokers (smoke more than 25 cigarettes per day; usually smoke within thirty minutes of awakening in the morning; and report smoking even when ill with a cold or minor respiratory complaint); b) are psychologically dependent (generally individuals who smoke as a means of affect regulation, stress management, or to help them cope with social interaction); c) or have tried to quit on their own and failed. The smokers most difficult to treat may be candidates for nicotine chewing gum as an adjunct to comprehensive treatment. By contrast, smokers who are less biologically addicted, less psychosocially dependent, and first-time quitters are candidates for self-help or other brief interventions.

A review of the patient's previous best attempt to quit can be revealing. It may illustrate, for example, that he/she was unable to quit although he/she smoked less (suggesting biological addiction); or he/she quit for a period, but then slipped back into smoking when stressed, feeling angry, or depressed (suggesting psychological dependence).

Thus, it is possible for a physician to move patients in a step-wise hierarchical fashion through four possible levels of intensity of treatment (self-help, brief intervention, formal program, formal program plus nicotine gum). The least intrusive, least expensive options are attempted first, and if these fail (or if there is already a history of failure or severe dependence) then more intensive treatment protocols are used. Individuals can "cycle through" the various stages of contemplation, action, maintenance, relapsing, and renewed motivation over several months or years if necessary, and the physician can always continue to support, follow up, and encourage them to keep trying. It is well to remember that we are dealing with a severe addiction, and that there are no quick and easy prescriptive cures.

Self-Help and Minimal Interventions

In order to compare programs, it is useful to know that the spontaneous-quit rate in the general population is 1 to 3 per cent per year. It is important that the cumulative impact of even a 5 per cent per year quit rate can make an enormous public health impact if every physician in the United States is achieving this rate in his/her practice. The lofty goal of a smoke-free America by the year 2000 is quite possible. Data on the effectiveness of self-help programs is sparse. The American Lung Association program (Freedom From Smoking in Twenty Days) and a companion maintenance manual (A Lifetime of Freedom From Smoking) achieved a 20 per cent initial quit rate with 18 per cent not smoking at twelve-month follow-up.[9] Another study evaluated materials provided by the American Cancer Society and self-help books that are available in paperback and based on behavior modification. The material of the American Cancer Society tended to produce slightly better results when used alone, whereas both books did better when used in conjunction with meetings supervised by a psychologist. Overall abstinence was seven per cent at six months and 24 per cent in the psychologist-administered group using the book by Pomerleau & Pomerleau.[10]

Several studies suggest the potential power of brief intervention in physicians' offices. In one

study of 28 general practitioners, patients received one of four treatments: a) no intervention, b) questionnaire only, c) physician advice to quit, and d) advice to quit plus informational leaflet and a follow-up interview. Only the fourth condition resulted in significantly lower smoking rates at one year follow-up (5.1 per cent abstinent vs 0.3 per cent to 3.3 per cent in the other 3 groups).[11] The finding that physician advice is improved when follow-ups and support are provided, is consistent with behavioral principles.

In general, hypnosis, acupuncture, and brief commercial interventions are difficult to evaluate because of the absence of objective data. However, several studies suggest that both one-session hypnosis and acupuncture treatments can be effective for some patients, at least in the short run. It is a key issue with these brief forms of treatment that they may not provide follow-up or teach maintenance skills to prevent relapse after quitting (see below for the criteria with which to evaluate a comprehensive treatment program). An important additional factor in commercial programs is the qualifications and reputation of the leaders. Many programs use principles of behavior modification, but they rarely use MD or PhD level clinical psychologists or psychiatrists who are also fully trained in behavior modification. Thus, the quality of the programs can be very variable, although some have excellent "natural leaders" or less qualified technicians. If programs involving repeated sessions and ongoing support are available, these would be recommended over "one-shot" programs. Generally the better programs report a success rate of between 10 and 25 per cent at six month follow-up. Obviously the lighter, less-dependent smokers who are highly motivated to quit and have excellent family supports for quitting are the preferred candidates for a brief or minimal intervention. They are likely to be high-functioning individuals who need a "little help" to get them started, but can basically manage to quit and prevent relapse on their own.

Formal Treatment Programs

The best programs should address three main types of treatment and provide specific skills training for a) quitting, b) coping with acute withdrawal, and c) maintenance/relapse prevention training. If hypnosis or acupuncture are used, they should be combined with other behavioral skills in a multi-session treatment of at least 4 to 8 weeks duration. The most consistent and objective research data on treatment efficacy come from behavioral modification programs.

Behavioral approaches to quitting include nicotine fading, stimulus control, and aversive techniques. Nicotine fading involves switching to lower nicotine brand cigarettes and reducing the number of cigarettes smoked per day on a systematic basis over a period of three to five weeks. Gradual reduction of nicotine is designed to minimize withdrawal symptoms. Stimulus control involves rearranging the environment and the self to make smoking more and more difficult (remove all ashtrays, smoke only in one room of the house, buy packs, not cartons). Although aversive strategies are unlikely to be widely accepted by subjects, they have yielded some of the most successful outcomes. Aversive strategies may be justified when benefits outweigh the risks, and less aversive methods have already been tried unsuccessfully. Smoking rapidly until tolerance is reached (feelings of nausea and dizziness) is the most common aversive procedure. Since rapid smoking increases heart rate, carboxyhemoglobin, and other blood gases, there have been questions raised about its safety in patients with cardiovascular disease. Behavioral strategies for contending with acute withdrawal symptoms include relaxation and deep breathing techniques, use of coping images (e.g. imagine that an urge to smoke is a wave that rises in the ocean, reaches a crest and then crashes and dissipates itself against the shore — urges are like waves, they will pass in time if you wait them out, do not give in). Other techniques include teaching patients how to formulate positive self-statements and counteract negative or catastrophizing thoughts such as "if I don't have a cigarette this second I will go crazy." The patient is encouraged to substitute phrases such as "I won't go crazy, I can make it, I'll take a few deep breaths and get through the next hour."

Behavioral techniques for maintenance and prevention of relapse are of recent origin and hold much promise, since 60 per cent of those who quit smoking will relapse within the first three months of quitting.[12] Techniques for relapse prevention should include a detailed analysis of "high risk situations." These are people, places, or emotional states that the smoker feels are most likely to precipitate a return to smoking. Individuals are taught how to cope with these situations, using rehearsal and other techniques to resist temptation. If they should slip back to smoking (one or two cigarettes) then they are provided with techniques to prevent the slip from becoming a full-blown relapse. Comprehensive

behavioral programs consist of weekly and sometimes daily sessions over a period of four to 10 weeks with about equal time devoted to quitting and maintenance. Additional support and follow-up is usually provided during the critical three to six months after quitting, when people are most vulnerable to relapse (e.g. a telephone "hot line" for crisis intervention if a patient is about to slip or has just slipped). In general the better behavioral programs produce success rates of between 30 and 60 per cent with follow-up of up to 18 months. The more usual success rate is in the region of 20 to 50 per cent at 6-12 months follow-up.

Nicotine chewing gum is designed to help minimize withdrawal symptoms and bridge the gap between quitting and maintenance. Once cessation has been achieved, gradual withdrawal from the nicotine gum is dealt with separately.[13] Most clinical trials with nicotine gum have been conducted in conjunction with behavior modification treatment programs. It is not recommended that the gum be prescribed alone without a formal treatment program that is designed to combine it with other behavioral management techniques. Studies using the combination of gum plus behavior modification have reported promising success rates in the range of 30-60 per cent at six months follow-up. Gum may be particularly useful for the very heavy smoker who has repeatedly failed to quit with both self-help and intensive formal treatment. In general, very few individuals become addicted to the gum itself. There are contraindications for gum use listed by the manufacturer. The questions about the ultimate utility of the gum and the best methods of administration must await the results of current research.

When shopping around for programs, one should note how the success rates are computed. Generally, most good programs will report 50-95 per cent initial quit rates. These rates may be biased in that they are based on self-reporting alone and only on the clients who actually complete treatment. They may define a quit attempt very leniently (24 hours of not smoking), rather than the more conservative and acceptable 48 hours or seven days of abstinence. Furthermore research shows that 60-80 per cent of those who quit have relapsed within six months of treatment. We recommend that six or 12 month follow-up data are more important in evaluating success than initial quit rates, that all clients be included in the follow-up statistics (those who are missing should be counted as failures), and that at least one objective measure be used to corroborate self-reporting (expired carbon monoxide, saliva or serum cotinine or thyiocynate, or the validation of a friend or relative). While many behavioral programs conform to these criteria, commercial programs and others unfortunately do not use uniform or standard criteria to report success. Thus, the educated physician and consumer must be able to identify how success rates are computed in order to compare local programs. Cost, reputation, and qualifications of the program leaders should also be considered along with the quality of the statistics about program efficacy.

Conclusion

Even a small amount of physician time can make a large impact in helping patients to become motivated for quitting and then to take action, quit, and resist relapse. A step-care plan can be adopted for every smoker whether in the office practice or in the hospital. More time and effort are placed on high-risk individuals and those who are willing to contemplate change. Beyond physician advice (which is a *very powerful* intervention if given properly and firmly), there are self-help and comprehensive programs that can be used. Clinics specializing in behavioral medicine and risk-factor modification are available, with highly trained health psychologists to deal with the more recalcitrant patients.

It is important to assess patient characteristics before deciding on the appropriate intervention. Patients who are only contemplating change should receive a systematic program of education, discussion, and support in order to prepare them for action. They should not be pushed into action prematurely, so that they are quitting to satisfy other people rather than themselves. It may take time to move a "contemplator" into action, but with concerted effort it can be done.

Once an individual is ready to take action, the type of program is determined by his/her level of nicotine dependence, psychological dependence, and past history of attempts to quit. Those who are less dependent and have not tried to quit on their own should first try low-cost self-help programs or brief interventions in the physician's office or using adjunctive procedures such as hypnosis or acupuncture. If these strategies have already been attempted without success or if the individual is too dependent on cigarettes biologically or psychologically, then more formal

treatment programs of four to eight weeks duration should be considered. These programs should teach skills for quitting, managing acute withdrawal, and maintenance/preventing relapse. Programs that add nicotine chewing gum to behavior modification should be considered for the chronic and more "difficult-to-treat" smoker who has tried to quit repeatedly without success. Persistence is the key to success, since many smokers will try two to four times to quit before succeeding.

Thus, a cumulative, step-care approach to treatment is recommended. Helping patients to quit smoking will over the next 30 years make the single largest impact on reducing chronic disease and disability in the United States. The National Cancer Institute and the voluntary agencies have committed themselves to working for a smoke-free America by the year 2000. Physicians, psychologists, state departments of public health, industry, and health professionals in general can help to achieve this goal. Tobacco dependence is a serious disorder. If an individual continues to smoke despite the signs and symptoms of disease (CD, chronic obstructive pulmonary disease, cancer) formal psychotherapeutic evaluation or intervention should be considered. The new behavioral treatments that have been developed over the past decade lead to a renewed cautious optimism about this serious, life-threatening addictive disorder. Patients must be educated about how to find the right treatment. We must not ask them to throw away their crutches before their bodies and minds have been prepared so that they may walk freely again! A smoke-free America by the year 2000 is a worthy goal.

References

[1] American Psychiatric Association, (1980): Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Washington, DC.

[2] Abrams, DB, & Wilson, GT (1986): Habit disorders, alcohol, and tobacco dependence. Chapter in AJ Francis & RE Hales (Eds.), *The American Psychiatric Association: Annual Review, Psychiatric Update,* Vol. 5, American Psychiatric Press Inc.

[3] U.S. Department of Health and Human Services (1982): The Health Consequences of Smoking: Cancer: A report of the Surgeon General. US DHHS Publication No. (PHS) 82-50179.

[4] U.S. Department of Health and Human Services (1983b): The Health Consequences of Smoking: Cardiovascular Disease: A report of the Surgeon General.

[5] Sepkovec, DW, Haley, NJ, & Wynder, EL (1984): Thyroid activity in cigarette smokers. *Archives of Internal Medicine, 144.*

[6] Pomerleau, OF, & Pomerleau, CS (1984): Neuroregulators and the reinforcement of smoking: Towards a biobehavioral explanation. *Neuroscience & Behavioral Reviews, 8,* 503-513.

[7] Repace, JL & Lowrey, AH (1985): A quantitative estimate of nonsmokers' lung cancer risk from passive smoking. *Environment International, 11,* 3-22.

[8] DiClemente, CC, & Prochaska, JO (1982): Self-change smoking cessation and smoking behavior: A comparison of processes of change in cessation and maintenance. *Addictive Behaviors, 7,* 133-142.

[9] Davis, AL, Faust, R, Ordentlich, M (1984): Self-help smoking cessation and maintenance programs: A comparative study with 12 month follow-up by the American Lung Association. *American Journal of Public Health, 74,* 1212-1217.

[10] Pomerleau, OF, & Pomerleau, CS (1977): Break the smoking habit: A behavioral program for giving up cigarettes. Champaign, IL, Research Press.

[11] Russell, MAH, Wilson, C, Taylor, C et al. (1979): Effect of general practitioners' advice against smoking. *Behavioral Medicine Journal, 2,* 231-235.

[12] Marlatt, GA, & Gordon, J (1985): *Relapse Prevention.* New York, Guilford.

[13] Hughes, JR, Miller, SA (1984): Nicotine gum to help stop smoking. *JAMA, 20,* 2855-2858.

164 Summit Avenue
Providence, RI 02906

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

Dollars and Sense of Percutaneous Biopsy

Demonstrates the Cost Effectiveness of the Procedure

Landy P. Paolella, MD
John J. Cronan, MD
Gary S. Dorfman, MD
Alfredo R. Esparza, MD

The era of cost consciousness is upon us in the medical field. With the imposition of the Diagnosis Related Group (DRG) reimbursement policy, cost has become a major consideration in patient care. The role of the primary care physician in organizing a cost-effective diagnostic and therapeutic plan is increasing continuously. To accomplish this the physician must make efficient use of inpatient and outpatient diagnostic testing and time in hospital.

Landy P. Paolella, MD, is a Clinical Assistant Instructor, Brown University Program in Medicine Fellow, Interventional Radiology, at the Department of Diagnostic Radiology, Rhode Island Hospital.

John J. Cronan, MD, is a Clinical Assistant Professor at the Brown University Program in Medicine, and a Radiologist with the Department of Diagnostic Radiology, Rhode Island Hospital.

Gary S. Dorfman, MD, is a Clinical Assistant Professor at the Brown University Program in Medicine, and is Director of Radiology, Special Procedures, Rhode Island Hospital.

Alfredo R. Esparza, MD, is a Clinical Associate Professor at the Brown University Program in Medicine, and a Pathologist with the Department of Pathology, Rhode Island Hospital.

From the Departments of Diagnostic Radiology and Pathology, Rhode Island Hospital and Brown University Program in Medicine, Providence, Rhode Island 02902. Statistical Reviewer: Vincent Mor, PhD, Associate Professor, Brown University.

Percutaneous biopsy (PB) of thoracic, abdominal, and retroperitoneal masses is now an established, accepted diagnostic procedure which can be performed with safety and accuracy.[1-4] Computerized tomography (CT) and ultrasound have advanced visualization of organs and lesions far beyond the capabilities of fluoroscopy and plain film studies, expanding the sites available for biopsy.[1,3,5-10] Smaller, more efficient, less traumatic needles and improvements in cytological and histological processing and interpretation have resulted in an increased diagnostic yield with decreased risk to the patient.[11-13] Although PB has proved itself as a diagnostic tool, we are only now beginning to realize the potential contribution it can make to decreasing the cost of health care while maintaining optimum care of patients.

We describe herein the introduction of PB in a 715-bed hospital. The impact on medical practice and potential savings in cost of health care will be presented.

Materials and Methods

During the two-year period from July 1982 through June 1984, 144 radiologically guided PBs were performed at our institution. The data were obtained from a review of medical records. All biopsies were performed, utilizing either CT, ultrasound, or fluoroscopy. The choice of imaging modality employed for guidance was individually determined on the basis of the size and location of the lesion.

Results of biopsies were considered *true positives* if the pathology report was positive for malignant disease or consistent with the pre-biopsy diagnosis in suspected non-malignant mass lesions. Over 90 per cent of biopsies were performed for suspected malignant lesions. Confirmation was obtained through follow-up in 75 per

cent of cases; surgical proof was recorded in approximately 25 per cent of cases. *True negatives* were those biopsies showing benign tissue, confirmed either surgically or by follow-up. A biopsy read as positive for malignant disease which was subsequently proven benign was a *false positive.* A *false negative* result was a biopsy read as benign in an organ which was later shown, either surgically or through follow-up, to contain a malignant lesion. Diagnostic accuracy was defined as the sum of the true positives and true negatives as a percentage of the total number of biopsies performed. An indeterminate biopsy resulted from an inadequate amount of tissue being obtained or from tissue acquired which was pathologically non-diagnostic for technical reasons.

Results of biopsies for medical renal disease were assessed differently. A biopsy was considered positive if adequate tissue was obtained for a histopathologic diagnosis.

Data on derivation of cost: In our series no randomization was used to establish a radiologically studied group and a surgical control group. Instead, estimated charges were generated for each patient as if they were studied radiologically and surgically. Therefore, each patient acted as his/her own control. The surgical charge estimate per procedure was minimized, as it was based on the "ideal patient" (ie under 70 years of age with the assumption that no complications occurred during hospitalization) (Table 1).[14,15] Conversely, the radiology charge per procedure was somewhat inflated as we added the charge for an average stay of 1.5 days to each biopsy performed (Table 2). While only 20 of the 144 biopsied patients were admitted as short stay patients (average stay 36 hours) the charge for 1.5 hospital days was integrated into the radiological charge to simulate a "worst case" scenario. The radiological costs were based on the premise that CT was used as the imaging modality in all cases. This is the most expensive modality and results in further inflation of our radiological expenses.

Results

We performed 144 PBs on 144 patients over a two-year period, from July 1982 through June 1984 (Table 3). The patient population ranged in age from 8 through 82 years, with 109 inpatients, 15 outpatients, and 20 short stays.

Biopsies for medical renal disease obtained adequate tissue for diagnosis in 100 per cent of cases (22 patients). Of the remaining 122 biopsies for suspected malignant disease, *96 true positives* (79 per cent) and 13 *true negatives* (11 per cent) were recorded for an overall diagnostic accuracy rate of 90 per cent. No false-positives results were obtained, however, 9 false negatives (7 per cent) and 4 indeterminates (3 per cent) were noted. In biopsies for suspected malignant disease, CT guidance was used in 79 cases, while fluoroscopy was used in 29 and ultrasound in 14. CT was the most accurate modality for guidance in our hands, with an accuracy rate of 92 per cent as compared

Table 1. Estimated Charges for Open Surgical Biopsy

Organ	Surgeons' Fee[3]	Anesthesia Fee[3]	Average Length of Stay[4]	Operating Room/ Recovery Room[5]	Total
Kidney[1]	$ 429.00	$245.00	$2,215.00	$410/$60	$3,358.00
Kidney[2]	429.00	245.00	3,661.00	410/60	4,805.00
Liver	572.00	265.00	4,045.00	410/60	5,352.00
Biliary	715.00	265.00	4,045.00	410/60	5,495.00
Abdomen	715.00	245.00	3,819.00	410/90	5,279.00
Retroperitoneum	572.00	270.00	3,819.00	492/90	5,243.00
Pelvis	715.00	320.00	3,819.00	656/120	5,630.00
Chest:					
Lung	1,073.00	510.00	3,254.00	820/120	5,777.00
Mediastinum:					
Thoracotomy	1,073.00	560.00	3,254.00	984/120	5,991.00
Mediastinoscopy	787.00	310.00	1,672.00	492/90	3,351.00

[1] Medical Renal Disease
[2] Malignant Disease
[3] From Physicians' Fee Reference
[4] Computation based on semi-private room rate at study site institution ($226.00/day) times number of days of hospitalization obtained from the Hospital Utility Project, Federal Register.
[5] Based on average occupancy times noted in study site institution for each procedure listed.

Table 2. Comparison of Projected Radiological and Surgical Biopsy Charges With Actual DRG Reimbursements

Organ	Projected Radiological Charges			Surgical Charges[1]	DRG Information[4]	
	Ultrasound	Fluoroscopy[5]	CT[6]		Code Numbers	Reimbursement
Kidney[2]	$629.00	$509.00	$710.00	$3,358.00	315	$ 9,275.00
Kidney[3]	604.00	484.00	685.00	4,805.00	303	9,275.00
Liver	604.00	484.00	685.00	5,352.00	199	9,275.00
Biliary	659.00	539.00	740.00	5,495.00	199	9,275.00
Abdomen	659.00	539.00	740.00	5,279.00	400	10,388.00
Retroperitoneum	659.00	539.00	740.00	5,243.00	400	10,388.00
Pelvis	659.00	539.00	740.00	5,630.00	400	10,388.00
Chest:						
Lung	659.00	539.00	740.00	5,777.00	075	9,646.00
Mediastinum:	659.00	539.00	740.00			
Thoracotomy				5,991.00	075	9,646.00
Mediastinoscopy				3,351.00	077	6,678.00

[1] See previous Table for breakdown of charges.
[2] Medical Renal Disease
[3] Malignant Disease
[4] The DRG code listed for medical renal disease is for acute renal failure. For masses in organs and other body regions the code for a malignant mass was used, for in the vast majority of cases the masses were indeed malignant. From Hospital Utility Project, Federal Register, September, 1983. DRG's are hospital and organ specific.
[5] Based on 15-minute units of fluoroscopy time, not room occupancy time.
[6] Assumes contrast was administered.

to ultrasound and fluoroscopy which were 79 per cent and 83 per cent accurate respectively. Twelve complications (10 per cent) occurred in all, with 9 of these occurring in biopsies of the lung and mediastinum. Eight of these 9 thoracic complications were pneumothoraces, only 3 of which required percutaneous insertion of a chest tube by the radiologist, using a Heimlich valve.[16-18] Therefore, the complication rate for nonthoracic biopsies was 3 per cent. No mortalities resulted.

For specific results and diagnostic accuracy in individual organs and body regions refer to Table 3.

Discussion

PB avoids the expense of a surgical procedure and prolonged hospitalization.[19,20] Table 2 shows comparisons in costs for surgical vs radiological approaches to establishing a tissue diagnosis. The figures listed in the total surgical cost column reflect only the cost of a surgical intervention and the resulting hospital stay. The difference between the DRG reimbursement and the total surgical cost consists of the remaining cost of hospitalization (eg initial admission workup, daily laboratory and radiological examinations, physicians' visits, consultations, medications, intravenous fluids and cost of other ancillary services). These remaining expenses also can be lessened due to the shortened hospital stay which results from a PB. Presently, DRGs dictate only medicare reimbursements to hospitals. However, if the trend continues and other third party payers adopt this system of reimbursement, the pressure will increase on both clinicians and hospitals to seek the most cost effective means of diagnosing and treating patients.[19]

Due to the low incidence of complications in our series of patients, we believe that a larger number of biopsies can be performed on individuals as outpatients. More outpatient biopsies, together with the prospect of avoiding surgery, general anesthesia, and hospitalization, make PB increasingly appealing.

Table 4 demonstrates what we believe are the potential savings realized in our initial series of biopsies. These figures assume that patients would have had a surgical biopsy, if percutaneous techniques were not available. In our series of 144 patients, fully $608,610 could have been saved, assuming 100 per cent diagnostic accuracy. With the accuracy rate we achieved, $524,409 potentially could have been saved. The impact of these biopsy procedures on our institution and the potential effect on health care costs can best be addressed by reviewing the individual organ systems and body regions.

Renal: Prior to July 1982, nearly all renal biopsies were performed by the open techniques under general anesthesia. Today radiologists at our

Table 3.

Anatomic Site	Number of Patients				Statistical Analysis					Compli-cations
	Total	In Pts.	Out Pts.	Short Stays	*Accur. Rate %	TP	TN	FN	Indeter-minate	
Kidney										
Medical Renal Disease	22	10	3	9	100	22	0	0	0	0
Suspected Malignant Renal Disease	14	14	0	0	93	11	2	1	0	2[1]
Liver	34	25	5	4	88	27	3	2	2	0
Biliary	7	7	0	0	86	6	0	1	0	1[2]
Lung	20	17	0	3	85	15	2	3	0	8[3]
Mediastinum	9	8	1	0	78	7	0	1	1	1[4]
Abdomen/Pelvis	38	28	6	4	95	30	6	1	1	0

*There were no false positives in our series

[1] Minor retroperitoneal hemorrhage not requiring treatment

[2] Single episode of transient sepsis which responded well to IV fluids and antibiotics

[3] 1 episode of frank hemoptysis not requiring treatment; 7 pneumathoraces, 3 of which required percutaneous chest tube insertion by the radiologist

[4] Minor pneumothorax not requiring treatment

institution perform all renal biopsies utilizing cross-sectional imaging techniques. No complications developed in our medical group; and only two minor complications occurred in the malignant group, neither of which required treatment.

For medical renal disease the combination of CT guidance to provide visualization and accurate placement of needles, together with the use of 14 gauge needles, assures adequate tissue specimens. Our 100 per cent success rate for tissue recovery and establishing the correct diagnosis in medical renal disease demonstrates that the need for open renal biopsy to establish a histological diagnosis in these patients has disappeared. By referring to Table 4 it may be observed that for medical renal disease alone the potential saving in health care cost to our institution, in our series of 22 patients was $58,256.

Biopsies for suspected neoplastic renal disease are less commonly requested by clinicians, probably because of the accuracy and acceptability of positive angiograms and CT scans. However, retroperitoneal masses can compress and distort renal parenchyma, as well as parasitize the renal vasculature, contributing to false-positive CT scans and angiograms. A positive biopsy allows for appropriate diagnosis, staging, and therapeutic planning.

Biliary: Malignant tumors obstructing the distal segment of the biliary tree, whether they be of biliary or pancreatic origin, carry a dismal prognosis.[21-25] Surgical approaches for tissue acquisition in patients with a limited life expectancy can result in a prolonged hospitalization. Percutaneous biliary biopsies with fluoroscopic guidance can be performed easily and inexpensively when done concurrently with percutaneous transhepatic cholangiography and biliary drainage. The bile obtained during drainage can be sent for cytology, further increasing diagnostic yield.[26] The diagnosis of an obstructing neoplasm affecting the distal end of the common duct can be established, and in appropriate cases the patient can be discharged soon thereafter without surgery.

Liver: PB of the liver has been performed for many years by surgeons and gastroenterologists, largely without the guidance of modern imaging.[27, 28] With diffuse hepatic parenchymal disease, a non-directed biopsy is effective. However, when tissue is required from focal and particularly small hepatic lesions (eg focal metastases, hepatoma), direct visualization of the needle position within the mass is necessary for consistent results. The potential saving noted in our series of 34 liver biopsies was $139,637.

Chest: The chest is perhaps the area where percutaneous thin-needle biopsy can make the greatest impact in terms of cost saving per patient (Table 2). Pulmonary lesions, large and small, peripheral and central, as well as mediastinal lesions, can be biopsied with accuracy and with relatively little risk to the patient.[1, 16, 17, 29, 30] Although only one of our patients was biopsied as an outpatient and three as short stays in hospital, this procedure has been performed in other centers much more extensively on an outpatient basis with excellent results and without significant morbidity.[18, 31, 32] However, even when performed on an inpatient, the length of post-biopsy

hospital stay vs that of a thoracotomy is impressively shorter, with obvious resultant savings in the cost of health care.[18-20] The potential saving for 20 patients undergoing PB instead of thoracotomy in our hands is over $85,000 (Table 4). Avoiding mediastinoscopy in just nine patients in our group can save an additional $18,000 (Table 4). Our 15 per cent (3/20) rate of complications for pneumothorax, necessitating percutaneous insertion of a chest tube and a Heimlich valve, is consistent with previous reports.[1, 16, 17, 29, 30]

Thoracotomy is a costly and often unnecessary operative procedure for diagnosing the nature of central and peripheral lung nodules. Pulmonary lesions as small as 1.5 cm in diameter can now be biopsied utilizing CT guidance with high rates of accuracy.[1, 16, 17, 30] This improvement in non-operative staging will, it is hoped, enable selection of those patients suited for surgical resection, thus increasing survival. A decrease in hospitalization time and cost also will be realized in the non-surgical group, as unnecessary surgical intervention is avoided.

Summary

Although percutaneous fine needle biopsy (PCFN) is acknowledged as a safe and accurate method of establishing a histologic diagnosis, little attention has been given to its potential contribution to improving the cost effectiveness of medical care. We herein present the concept of PCFN biopsy as an economical method of establishing a tissue diagnosis that can have a significant impact on cost containment. Our data compare the individual dollar cost of PCFN versus surgical biopsy. We have reviewed individual components of the final cost. The cost of obtaining a tissue diagnosis via PCFN biopsy consists of the physician's fee, the cost for the use of the imaging modality, equipment cost, and the pathology processing and interpretation fees. This is compared with the surgical costs which include professional fees for both the surgeon and the anesthesiologist, operating room and recovery room costs, hospitalization costs and the pathology interpretation and processing fees. Our calculated potential saving of over $520,000 for establishing a tissue diagnosis by PCFN biopsy as against surgery in our series of 144 patients over a two-year period should establish the importance of this procedure as a cost containment measure.

The present trend of medical care is toward more cost-effective diagnosis and treatment without compromising quality. This goal can be achieved in part by increasing outpatient diagnostic studies, shortening hospital stays, and avoiding unnecessary surgery.

With PB, accurate diagnosis on tissue obtained can now be made in 80 to 100 per cent of cases, depending on the organ involved, without the increased morbidity, mortality, or expense of surgery. Biopsies can be performed on outpa-

Table 4. Comparison of Charges and Potential Savings For This Series

Area Biopsied	Number of Biopsies	Estimated Charge For Radiological Biopsy[2]	Estimated Charge For Surgical Biopsy	Potential Savings (Assuming 100% Accuracy)	Potential Savings With Our Accuracy Rate
Kidney					
Medical Renal Disease	22	$ 15,620.00	$ 73,876.00	$ 58,256.00	$ 58,256.00 (100%)[3]
Malignant Disease	14	9,590.00	67,270 00	57,680.00	53,642.00 (93%)
Liver	34	23,290.00	181,968.00	158,678.00	139,637.00 (88%)
Biliary	7	5,180.00	38,465.00	33,285.00	28,625.00 (86%)
Lung	20	14,800.00	115,540.00	100,740.00	85,629.00 (85%)
Mediastinum[1]	9	6,660.00	30,159.00	23,499.00	18,329.00 (78%)
Abdomen/Pelvis	38	28,120.00	204,592.00	176,472.00	167,648.00 (95%)
TOTAL	144	$103,260.00	$711,870.00	$608,610.00	$524.409.00 (91%)

[1] Based on mediastinoscopy
[2] Based on cost of CT as imaging modality
[3] Numbers in parentheses represent our diagnostic accuracy rate in this specific organ or body region.

tients or on patients admitted for 24 to 48 hours. Inpatients can have their stays shortened by being spared an operative procedure with its increased problems.

We have demonstrated the potential savings available utilizing PB instead of surgery to establish a tissue diagnosis. A potential criticism of our data is that we compared surgical inpatients with a mixture of radiological inpatients, outpatients, and patients in hospital for short stays. We compensated for this by adding 1.5 hospital days to the radiological group, as well as by using CT (the most expensive modality) in our calculations. Although these may still not be exact comparisons, we feel the potential for savings is obvious. The DRG figures are listed to give a relative comparison of what an inpatient diagnostic hospitalization can cost. We do not suggest that this is the reimbursement for a short hospital stay or outpatient biopsy, as DRGs pertain only to inpatient procedures.

For the full impact of PB to be felt, it must be more widely available, not only in large medical centers, but in community hospitals. The introduction of PB techniques in the community hospitals is an integral part of the overall goal of providing the population at large with "state-of-the-art" medical care. Community hospitals without a CT-scanning facility can still offer PB, utilizing ultrasound or fluoroscopy.

The time for more widespread use of PB has arrived. Its impact on the diagnostic workup and treatment plan of practicing clinicians, with a resultant saving to the entire health care system, should follow with little delay. Our experience with this technique indicates its rapid acceptance and impact on patient care.

Acknowledgement

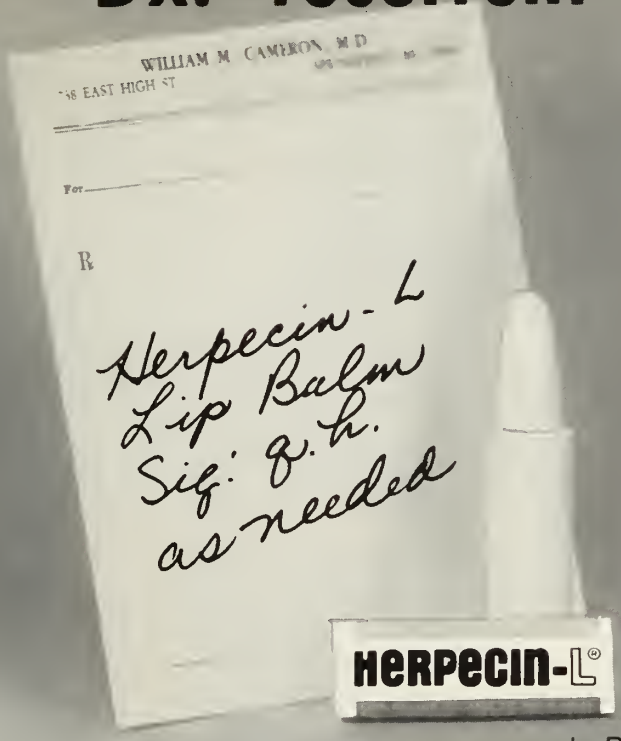
The authors wish to thank Gayle Pascetta for her assistance in preparation of the manuscript.

References

1 Gobien RP, Stanley JH, Vujic I, et al. Thoracic biopsy: CT guidance of thin needle aspiration. AJR 1984;142:827-830.
2 Greene R. Transthoracic needle aspiration biopsy. In: Athanasoulis CA, Pfister RC, Greene RE, Roberson GH, eds. Interventional radiology. Philadelphia: Saunders, 1982:587-634.
3 Ferrucci JT Jr, Wittenberg J. CT biopsy of abdominal tumors: aids for lesion localization. Radiology 1978;129:739-744.
4 Kline TS, Neal HS. Needle aspiration biopsy: A critical appraisal eight years and 3,267 specimens later. JAMA 1978;239:36-39.
5 Bernardino ME. Percutaneous biopsy. AJR 1984;142:41-45.
6 Sundaram M, Wolverson MK, Heiber E, et al. Utility of CT guided abdominal aspiration procedures. AJR 1982;139:1111-1115.
7 Buonocore E, Skipper GJ. Stirrable real time sonographically guided needle biopsy. AJR 1981;136:387-392.
8 Grant EG, Richardson JD, Smirniotopoulos JG, Jacobs NM. Fine needle biopsy directed by real time sonography: technique and accuracy. AJR 1983;141:29-32.
9 Nosher JL, Plafker J. Fine needle aspiration of the liver with ultrasound guidance. Radiology 1980;136:177-180.
10 Reid MH. Real time sonographic needle biopsy guide. AJR 1983;140:162-163.
11 Wittenberg J, Mueller PR, Ferrucci JT Jr, et al. Percutaneous core biopsy of abdominal tumors using 22 gauge needles: further observations. AJR 1982;139:75-80.
12 Isler RJ, Ferrucci JT Jr, Wittenberg J, et al. Tissue core biopsy of abdominal tumors with a 22 gauge cutting needle. AJR 1981;136:725-728.
13 Ferrucci JT Jr, Wittenberg J, eds. Interventional radiology of the abdomen. Baltimore: Williams & Wilkins, 1981:117.
14 Federal Register, Department of Health and Human Services 1983.
15 Physicians' Fee Reference, Wisconsin, 1983.
16 Westcott JL. Direct percutaneous needle aspiration of localized pulmonary lesions: results in 422 patients. Radiology 1980;137:31-35.
17 Westcott JL. Percutaneous needle aspiration of hilar and mediastinal masses. Radiology 1981;141:323-329.
18 Stevens GM, Jackman RJ. Outpatient needle biopsy of the lung: its safety and utility. Radiology 1984;151:301-304.
19 Kaminsky DB. Aspiration biopsy in the context of the new medicare fiscal policy. ACTA Cytologica 1984;28(3):333-336.
20 Gobien RP, Bouchard EA, Gobien BS, et al. Thin needle aspiration biopsy of thoracic lesions: impact on hospital charges and patterns of patient care. Radiology 1983;148:65-67.
21 Schantz SP, Schickler W, Evans TK, Coffey RJ. Palliative gastroenterostomy for pancreatic cancer. American Journal of Surgery 1984;147:793-796.
22 Jain KM, Brief DK, Nozick J. Carcinoma of the pancreas: fifteen years experience. American Journal of Surgery 1979;45:15-20.
23 Alexander F, Rossi RL, O'Bryan M, et al. Biliary carcinoma: a review of 109 cases. American Journal of Surgery 1984;147:503-508.
24 Braasch JW, Kune GA, Warren KW. Malignant neoplasms of the bile ducts. Surgical Clinics of North America 1967;47:627-638.
25 Lee YT, Tatter D. Carcinoma of the pancreas and periampullary structures. Pattern of metastases at autopsy. Archives of Pathology and Laboratory Medicine 1984;108:584-587.
26 Harell GS, Anderson MF, Berry PF. Cytologic bile examination in the diagnosis of biliary duct neoplastic strictures. AJR 1981;137:1123-1126.
27 Haaga JR, Vanek J. Computed tomographic guided liver biopsy using the Menghini needle. Radiology 1979;133:405-408.
28 Perrault J, McGill DB, Ott BJ, Taylor WF. Liver biopsy: complications in 1000 inpatients and outpatients. Gastroenterology 1978;74:103-106.
29 vanSonnenberg E, Lin AS, Deutsch AL, Mattrey RF. Percutaneous biopsy of difficult mediastinal, hilar and pulmonary lesions by computed tomographic guidance and a modified coaxial technique. Radiology 1983;148:300-302.
30 Berquist TH, Bailey PB, Cortese DA, Miller WE. Transthoracic needle biopsy. Accuracy and complications in relation to location and type of lesion. Mayo Clinic Proceedings 1980;55:475-481.
31 Meyer JE, Gandbhir LH, Milner LB, McLaughlin MM. Percutaneous aspiration biopsy of nodular lung lesions. Journal of Thoracic and Cardiovascular Surgery 1977;73:787-791.
32 Jackson R, Coffin LH, DeMeules JE, Neer DB, et al. Percutaneous needle biopsy of pulmonary lesions. American Journal of Surgery 1980;139:586-590.

593 Eddy Street
Providence, RI 02902

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

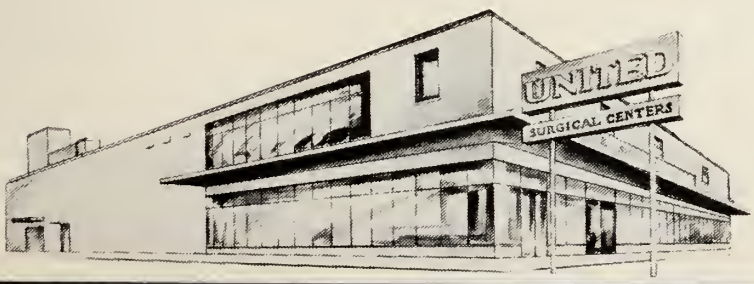
OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



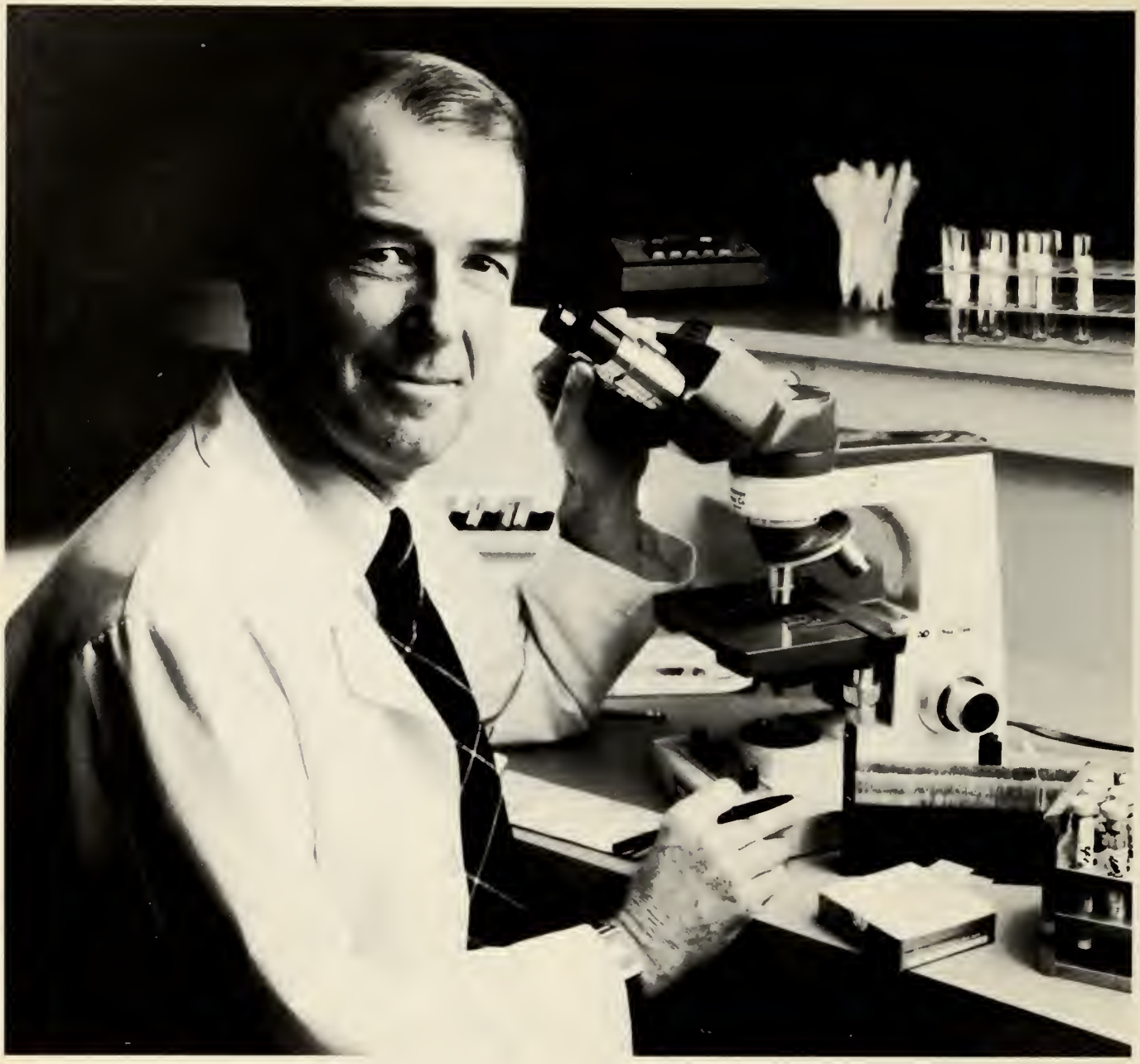
We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line



Dr. McLeod is losing his patients.
One by one.

The simple fact is, Dr. McLeod's billing service isn't doing as good a job as he assumes it is. His patients are becoming annoyed with the frequency of billing errors. Which leaves Dr. McLeod with a problem he doesn't even know he has.

The mistake that our hypothetical Dr. McLeod made is no myth. In reality, many physicians believe there are no significant differences between billing services. Different software packages, perhaps. Price. But beyond that, a billing service . . . is a billing service.

The truth is, it makes a *big* difference who handles your practice billing. Things can and do go wrong—like misbilling and mismanaged or even unprofessional collection procedures. These and other problems not only cost a practice financially, but can impact on patient satisfaction and goodwill, which is perhaps most costly of all.

If you really don't want to worry about billing, take a close look at how you do your billing now. And then call us. We'll be pleased to demonstrate our stability and track record. To explain our billing and collection procedures and our patient relations standards. And to show you how our customized services can meet your practice needs and improve your cash flow.

Call us soon. Because you have everything to lose.

pms
Professional
Management
Services, Inc.

(401) 521-6310

Boston
W. Springfield, MA
Philadelphia
Providence
Hartford

A Nursing Home
Striving to Provide
The Ultimate in Nursing Home
Service

100 Wampanoag Trail *East Providence*
401/438-4275

THE DEPARTMENT OF ORTHOPAEDICS
AND REHABILITATION
RHODE ISLAND HOSPITAL
PRESENTS

THE SEVENTH ANNUAL KENNETH G. BURTON LECTURE

RICHARD G. EATON, M.D.
CLINICAL PROFESSOR OF ORTHOPAEDIC SURGERY
COLUMBIA COLLEGE OF PHYSICIANS AND SURGEONS
CHIEF, HAND SERVICE
ST. LUKE'S — ROOSEVELT HOSPITAL
NEW YORK, NEW YORK

"INTERPOSITION TENDON GRAFTS FOR CARPAL BONE REPLACEMENT"

"AN APPROACH TO THE TREATMENT OF ALL STAGES OF BASAL JOINT DISEASE"

FRIDAY, MAY 15, 1987
8:00 A.M.
GEORGE AUDITORIUM
RHODE ISLAND HOSPITAL

DEPARTMENT OF ORTHOPAEDICS
BROWN UNIVERSITY PROGRAM IN MEDICINE

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

This space contributed as a public service.

$500,000,000 OF RESEARCH HELPED CLIFF SHAW PLAY BASEBALL AT AGE 85.

In November 1973, Cliff Shaw was stricken with cancer.

Fortunately, it was detected early enough. And with surgery, Cliff was able to continue living a healthy, active life.

There was a time when such a diagnosis was virtually hopeless.

But today, cancer is being beaten. Over the years, we've spent $500,000,000 in research. And we've made great strides against many forms of cancer.

With early detection and treatment, the survival rate for colon and rectal cancer can be as high as 75%. Hodgkin's disease, as high as 74%. Breast cancer, as high as 90%.

Today, one out of two people who get cancer gets well. It's a whole new ball game.

AMERICAN CANCER SOCIETY®

Help us keep winning.

CONFIRMED

CONFIRMED BY CLINICAL EVIDENCE

ZANTAC® 150 h.s.

ranitidine HCl/Glaxo 150 mg tablets

EFFECTIVE MAINTENANCE THERAPY

for healed duodenal ulcer patients

CONFIRMED

In two randomized, double-blind, and well-controlled clinical trials, ZANTAC 150 mg h.s. significantly superior to cimetidine 400 mg h.s. for maintenance therapy in healed duodenal ulcers.

Percent of patients with observed duodenal ulcer recurrence

		0-4 months	0-8 months	0-12 months	No. patients
USA[1]	ranitidine 150 mg h.s.	9%	14%*	16%†	60
	cimetidine 400 mg h.s.	23%	34%	43%	66
UK, Ireland, Australia[2]	ranitidine 150 mg h.s.	8%‡	14%‡	23%‡	243
	cimetidine 400 mg h.s.	21%	34%	37%	241

*p=0.02
†p=0.01
‡p≤0.004
%=life-table estimates
All patients were permitted prn antacids for relief of pain.

These two trials used the currently recommended dosing regimen of cimetidine (400 mg h.s.) and ranitidine (150 mg h.s.). A comparison of other dosing regimens has not been studied.

The studied dosing regimens are not equivalent with respect to the degree and duration of acid suppression or suppression of nocturnal acid.

The superiority of ranitidine over cimetidine in these trials indicates that the dosing regimen currently recommended for cimetidine is less likely to be as successful in maintenance therapy.

Convenient once-a-night dose with a

low incidence of side effects[3]

Headache, sometimes severe, seems to be related to ranitidine administration. Other side effects have been reported; for a complete listing, see the **ADVERSE REACTIONS** section in the Brief Summary.

No significant interference with the hepatic cytochrome

P-450 enzyme system at recommended doses

ZANTAC 150 mg has no significant drug interactions with theophylline, phenytoin, or warfarin. The bioavailability of certain medications whose absorption is dependent on a low gastric pH may be altered when ZANTAC or other medications that decrease gastric acidity are administered.

Zantac® 150

ranitidine HCl/Glaxo 150 mg tablets

One tablet at bedtime
for maintenance

See next page for references and
Brief Summary of Product Information.

Glaxo / ROCHE®

CONFIRMED

Zantac® 150

ranitidine HCl/Glaxo 150 mg tablets

One tablet at bedtime for maintenance therapy in healed duodenal ulcer patients

References:

1. Silvis SE, Griffin J, Hardin R, et al: Final report on the United States multicenter trial comparing ranitidine to cimetidine as maintenance therapy following healing of duodenal ulcer. *J Clin Gastroenterol* 1985;7(6):482-487.
2. Gough KR, Korman MG, Bardhan KD, et al: Ranitidine and cimetidine in prevention of duodenal ulcer relapse: A double-blind, randomised, multicentre, comparative trial. *Lancet* 1984;ii 659-662.
3. Data available on request, Glaxo Inc.

ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:

1. Short-term treatment of **active duodenal ulcer.** Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD).** Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of therapy.

In active duodenal ulcer, active, benign gastric ulcer, hypersecretory states, and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Although recommended doses of ZANTAC do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Lack of experience to date precludes recommending ZANTAC for use in children or pregnant patients. Since ZANTAC is secreted in human milk, caution should be exercised when administered to a nursing mother.

ADVERSE REACTIONS: Headache, sometimes severe, seems to be related to ZANTAC® administration. Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, premature ventricular beats, and arthralgias. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients.

In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

There have been rare reports of reversible leukopenia, granulocytopenia, thrombocytopenia, and pancytopenia.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Incidents of rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NOC 0173-0393-40) and unit dose packs of 100 tablets (NOC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NOC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

© Copyright 1983, Glaxo Inc. All rights reserved. October 1986

Glaxo

Glaxo Inc.
Research Triangle Park, NC 27709

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl)

after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl)
LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information.

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

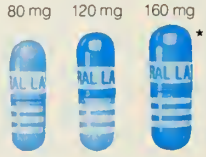
Propranolol is not significantly dialyzable.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES



INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension. It may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely. If INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System: lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985;145:1321-1323.

6412/187

Ayerst® AYERST LABORATORIES
New York, NY 10017

© 1986 Ayerst Laboratories

Motrin® 800 TABLETS mg

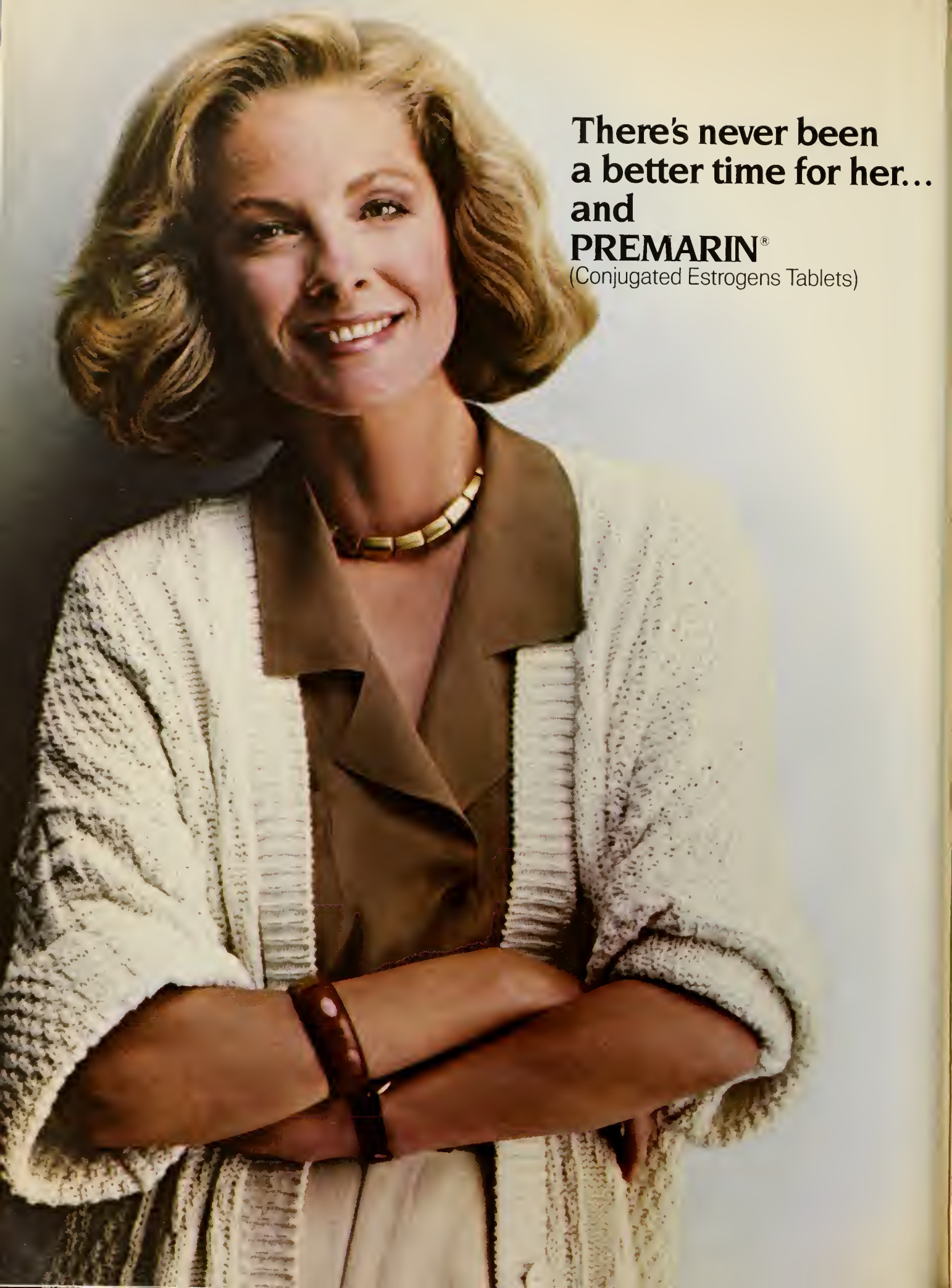
ibuprofen

Extra strength
Convenience
Economy

Upjohn 100 A Century of Caring 1886·1986

©1986 The Upjohn Company

J-6138 January 1986


There's never been
a better time for her...
and
PREMARIN®
(Conjugated Estrogens Tablets)

Now the evidence looks better than ever

Significantly reduced risk of endometrial hyperplasia

Endometrial hyperplasia was significantly reduced when progestin was added to PREMARIN therapy for more than ten days a month.[1-4] The risk of endometrial hyperplasia may also be reduced through cyclic administration of unopposed, low-dose PREMARIN.

Effect on lipids—an important feature

PREMARIN used alone does not adversely affect lipid levels. In fact, a clinical study has shown a significant increase in HDL cholesterol—from 49.7 mg/dL to 56.4 mg/dL—and decrease in LDL cholesterol—from 165.1 mg/dL to 138.1 mg/dL—after one year of therapy with PREMARIN, 0.625 mg.[5]

Low-dose control of menopausal symptoms*

PREMARIN effectively relieves vasomotor symptoms, such as hot flashes. When estrogen deficiency is limited to atrophic vaginitis, PREMARIN® (conjugated estrogens) Vaginal Cream restores the vaginal environment to its premenopausal state.

The most widely used, most extensively studied estrogen worldwide.

PREMARIN®
(Conjugated Estrogens Tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms

PREMARIN®
(Conjugated Estrogens Tablets)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

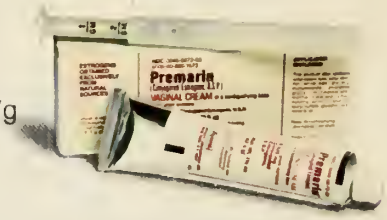
The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(Conjugated Estrogens)

Vaginal Cream

0.625mg/g



BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1 ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2 ESTROGENS SHOULD NOT BE USED DURING PREGNANCY

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP). Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding; spotting; change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis; change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine, dizziness; mental depression; chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria, edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically.* Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis—0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Whitehead MI, Townsend PT, Pryse-Davies J, et al: Effects of estrogens and progestins on the biochemistry and morphology of the postmenopausal endometrium. *N Engl J Med* 1981;305:1599-1605. **2.** Paterson MEL, Wade-Evans T, Sturdee DW, et al: Endometrial disease after treatment with oestrogens and progestogens in the climacteric. *Br Med J* 1980;280:822-824. **3.** Magos AL, Brincat M, Studd JWW, et al: Amenorrhea and endometrial atrophy with continuous oral estrogen and progestogen therapy in postmenopausal women. *Obstet Gynecol* 1985;67:496-499. **4.** Whitehead MI, Lane G, Siddle N, et al: Avoidance of endometrial hyperstimulation in estrogen-treated postmenopausal women. *Semin Reprod Endocrinol* 1983;1:1;41-52. **5.** Barnes RB, Roy S, Lobo RA: Comparison of lipid and anorogen levels after conjugated estrogen or depo-medroxyprogesterone acetate treatment in postmenopausal women. *Obstet Gynecol* 1985;66:216-219.

© 1986 Ayerst Laboratories

Ayerst® AYERST LABORATORIES
New York, NY 10017

T6194/BB6

ROCHE ME MEDICATION EDUCATION

The *New* Roche Product Books

- **Offer a supplement to, not a substitute for, patient contact**
- **Support your specific instructions to the patient**
- **Provide a permanent general reinforcement of your oral counseling**

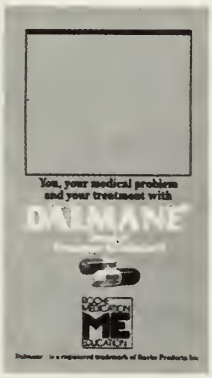
An ongoing Roche commitment to patient education

Roche has always believed that knowledge is each individual's key to good health and has long been committed to providing health care information to both professionals and the public. However, we have also always believed that the health care professional is and should be the prime source of medication information to patients. The Roche Medication Education (ME) program, begun in 1978, is one example of this commitment.

In the past seven years, over 50 million "WHAT IF" and "HOW TO" booklets have been provided by Roche for distribution to patients by physicians and other health care professionals.

Because you are the prime source of medication information for your patients, we invite you to look over the booklets listed below and request a complimentary supply of those applicable to your practice.

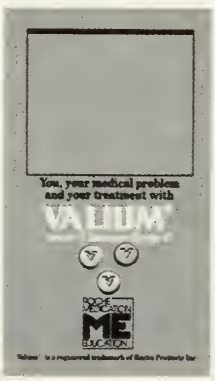
Complete the coupon and mail it to Professional Services Department, Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, New Jersey 07110.



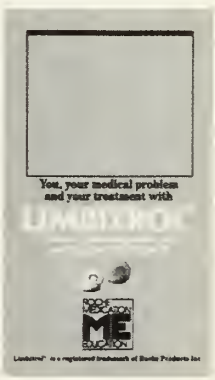
☐

☐

☐



☐



☐

NAME

STREET ADDRESS

CITY STATE ZIP

ROCHE®

Medicines that matter
from people who care

ROCHE MEDICATION ME EDUCATION

We Wrote the Books on Patient Medication Education...

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

You, your medical problem and your treatment with

DALMANE®

brand of flurazepam HCl/Roche ©

You, your medical pr
and your treatment

LIBRIU

brand of

You, your medical problem and your treatment with

BACTRIM™

brand of trimethoprim and sulfamethoxazole/Roche

You, your medical problem and your treatment with

VALIUM®

brand of diazepam/Roche ©

You, your medical problem and your treatment with

LIMBITROL®

brand of chlordiazepoxide and amitriptyline HCl/Roche ©

ROCHE®

Copyright ©
1986 by Hoffmann-La Roche Inc.
and Roche Products Inc.
All rights reserved.

To order a complimentary supply of Roche Product Books, please see preceding page.

Rhode Island Medical Journal

April 1987
Volume 70, Number 4

DISPLAY SHELF

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
APR 27 1987

Francis B. Sargent, MD shares his experience as head of the Defense Committee. *See page 179.*

CONTRIBUTIONS

163 Issues in the Management of Recurrent Headache

173 Chordomas: A Review

179 Sixteen Years As Defense Committee Chairmanship

161 EDITORIALS

181 BOOK REVIEW

169 INFORMATION FOR AUTHORS

AIM HIGH

A PRESCRIPTION FOR PHYSICIANS

BOTHERED BY:

- ★ Too much paperwork?
- ★ The burden of office overhead?
- ★ Malpractice insurance costs?
- ★ Not enough time for the family?
- ★ No time to keep current with technology and new methods?
- ★ No time or money for professional development?

JOIN THE AIR FORCE MEDICAL TEAM; WE'LL PROVIDE THE FOLLOWING:

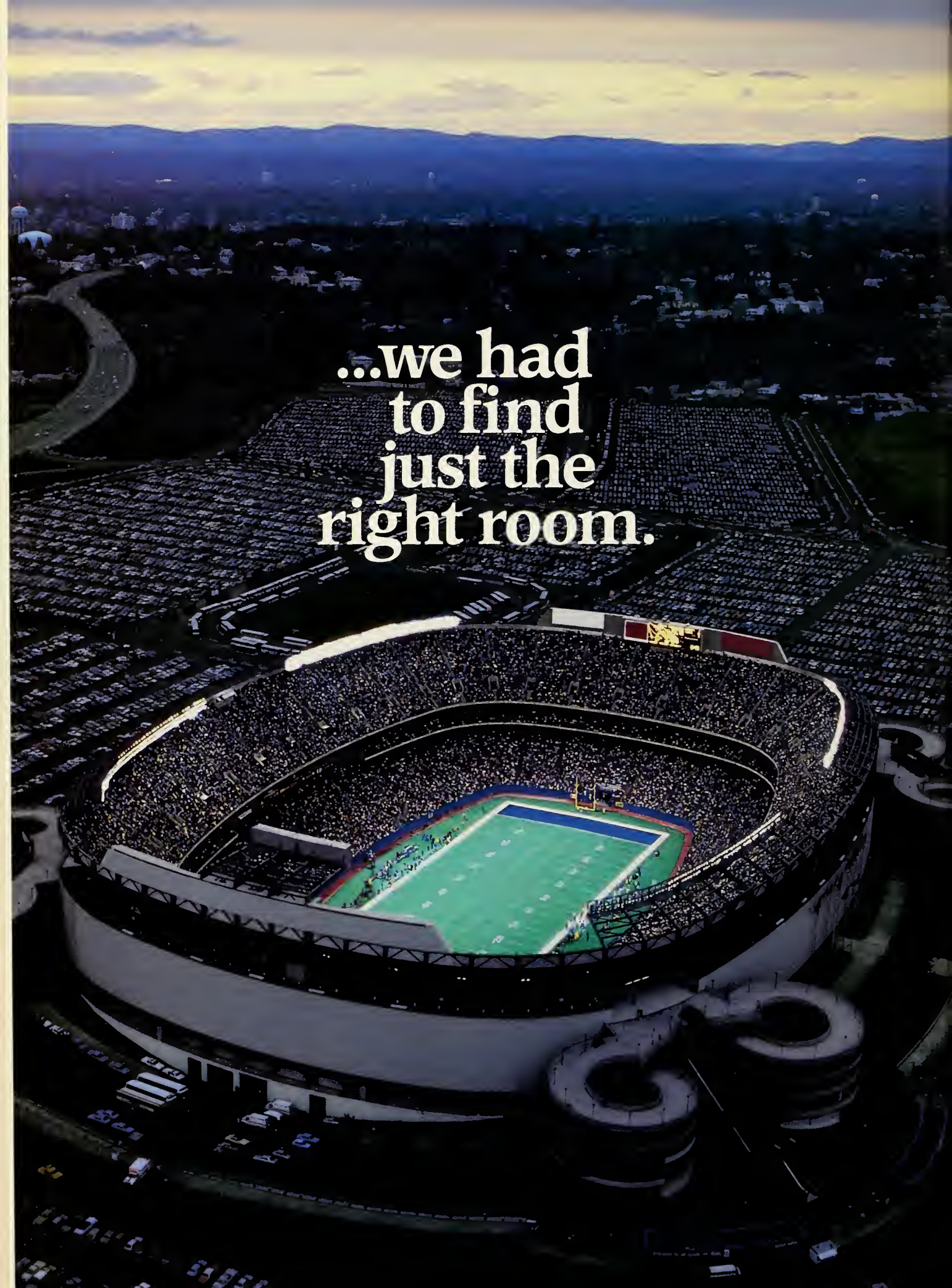
- ★ Competent and dedicated professional staff.
- ★ Time for patients and for keeping professionally current.
- ★ Financial security, a generous retirement for those who qualify.
- ★ If qualified, unlimited professional development.
- ★ Medical facilities all around the world.
- ★ 30 days of vacation with pay each year.
- ★ Complete medical and dental care.
- ★ Low cost life insurance.

Want to find out more? Contact your nearest Air Force recruiter for information at no obligation. Call

Ssgt A. J. Avila
401-528-4044 collect

AIR FORCE

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...


...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were controlled merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl)
LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. Inderal LA is formulated to provide a sustained release of propranolol hydrochloride. Inderal LA is available as 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg for mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

The mechanism of the antihypertensive effect of INDERAL has not been established. Among the factors that may be involved in contributing to the antihypertensive action are (1) decreased cardiac output, (2) inhibition of renin release by the kidneys, and (3) diminution of tonic sympathetic nerve outflow from vasomotor centers in the brain. Although total peripheral resistance may increase initially, it readjusts to or below the pretreatment level with chronic use. Effects on plasma volume appear to be minor and somewhat variable. INDERAL has been shown to cause a small increase in serum potassium concentration when used in the treatment of hypertensive patients.

In angina pectoris, propranolol generally reduces the oxygen requirement of the heart at any given level of effort by blocking the catecholamine-induced increases in the heart rate, systolic blood pressure, and the velocity and extent of myocardial contraction. Propranolol may increase oxygen requirements by increasing left ventricular fiber length, end diastolic pressure and systolic ejection period. The net physiologic effect of beta-adrenergic blockade is usually advantageous and is manifested during exercise by delayed onset of pain and increased work capacity.

In dosages greater than required for beta blockade, INDERAL also exerts a quinidine-like or anesthetic-like membrane action which affects the cardiac action potential. The significance of the membrane action in the treatment of arrhythmias is uncertain.

The mechanism of the antimigraine effect of propranolol has not been established. Beta-adrenergic receptors have been demonstrated in the pial vessels of the brain.

Beta receptor blockade can be useful in conditions in which, because of pathologic or functional changes, sympathetic activity is detrimental to the patient. But there are also situations in which sympathetic stimulation is vital. For example, in patients with severely damaged hearts, adequate ventricular function is maintained by virtue of sympathetic drive which should be preserved. In the presence of AV block, greater than first degree, beta blockade may prevent the necessary facilitating effect of sympathetic activity on conduction. Beta blockade results in bronchial constriction by interfering with adrenergic bronchodilator activity which should be preserved in patients subject to bronchospasm.

Propranolol is not significantly dialyzable.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES

80 mg 120 mg 160 mg

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely; or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. *General.* Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. lightheadedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal. nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. bronchospasm.

Hematologic. agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. alopecia. LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL tablets to INDERAL LA capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg for mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg *once* daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three to seven day intervals until optimum response is obtained. Although individual patients may respond at any dosage level, the average optimum dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimum migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximum dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985;145:1321-1323.

6412 187

Ayerst® AYERST LABORATORIES
New York, NY 10017

© 1986 Ayerst Laboratories

ZOVIRAX®
(acyclovir)
CAPSULES

Prevent genital herpes recurrences month after month with daily therapy.

(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

Please see last page of this advertisement for brief summary of prescribing information.

ZOVIRAX®
(acyclovir)
CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes, as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next page.

Prevent recurrences month after month*

ZOVIRAX® (acyclovir) CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psychosocial difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies, the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤10 ml/min/1.73/m².

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200"- Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

---

*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

Wellcome | Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Copr. © 1986 Burroughs Wellcome Co. All rights reserved. 86-ZOV-5

HOME NURSING CARE

Private Duty Nursing

* REGISTERED NURSES
* LICENSED PRACTICAL NURSES
* NURSE AIDES
* HOMEMAKERS
* HOME HEALTH AIDES

When Home Care Is Needed

Please Call . . .

CATHLEEN NAUGHTON ASSOCIATES

Employes Bonded and Insured

cna

(401) 751-9660

Available 7 days a week
24 hours a day.

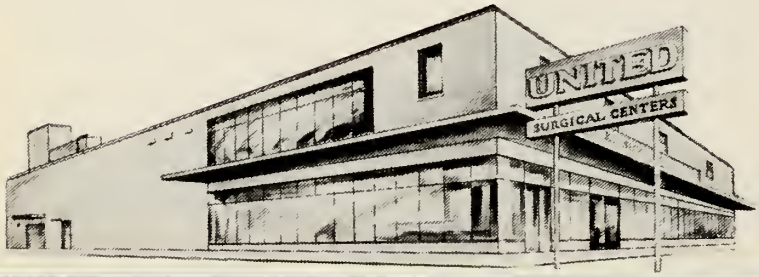
PROFESSIONAL OFFICE SUITE FOR LEASE NORTH PROVIDENCE

Centrally Located
Approximately 2000 sq. ft.
New Building — Parking
Adjacent to Free-Standing
Ambulatory Care Office
Call Mrs. Merola
353-6362
9am-3pm Mon.-Fri.

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
APR 27 1987

April 1987
Volume 70, Number 4

Rhode Island Medical Journal

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Guy A. Settipane, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

***Edward R. Feller, MD**

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Peter D. T. Clarisse, MD
President

Richard G. Bertini, MD
President-Elect

Milton W. Hamolsky, MD
Secretary

Kenneth E. Liffmann, MD
Treasurer

Herbert Rakatansky, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

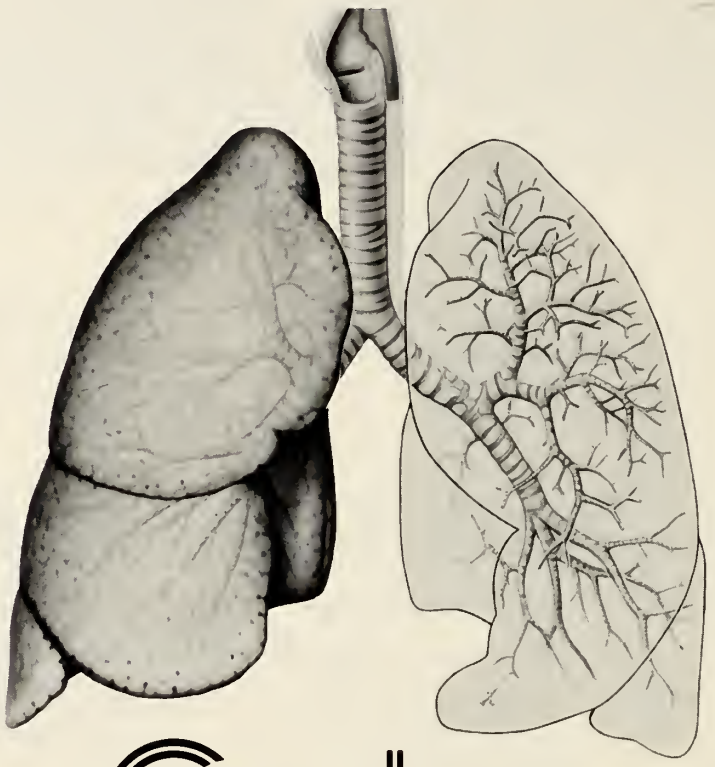
Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, H influenzae, Streptococcus pneumoniae, Streptococcus pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Note: Ceclor® is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae,* and *S. pyogenes* (group A beta-hemolytic streptococci).

Contraindications: Known allergy to cephalosporins.

Warnings: CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:

- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- In renal impairment, safe dosage of Ceclor may be lower than that usually recommended. Ceclor should be administered with caution in such patients.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:

- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, erythema multiforme, serum-sickness-like reactions): 1.5%; usually subside within a few days after cessation of therapy. These reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%.

Abnormalities in laboratory results of uncertain etiology

- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children)
- Abnormal urinalysis; elevations in BUN or serum creatinine
- Positive direct Coombs' test
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly)

© 1986, ELI LILLY AND COMPANY [060485LR]

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

600332

TABLE OF CONTENTS

161 **EDITORIALS**

The Trials of Blue Cross and Blue Shield

Seebert J. Goldowsky, MD

More on Tobacco

Seebert J. Goldowsky, MD

181 **BOOK REVIEW**

CONTRIBUTIONS

163 **Issues in the Management of Recurrent Headache**

Non-Pharmacological Treatment Offers Relief to Many Victims

Virginia Attanasio, PhD
Joanne L. Fowler, PhD
Michael J. Follick, PhD
Richard J. Perry, MD

173 **Chordomas: A Review**

Early Diagnosis and Complete Removal Offer Potential for Cure

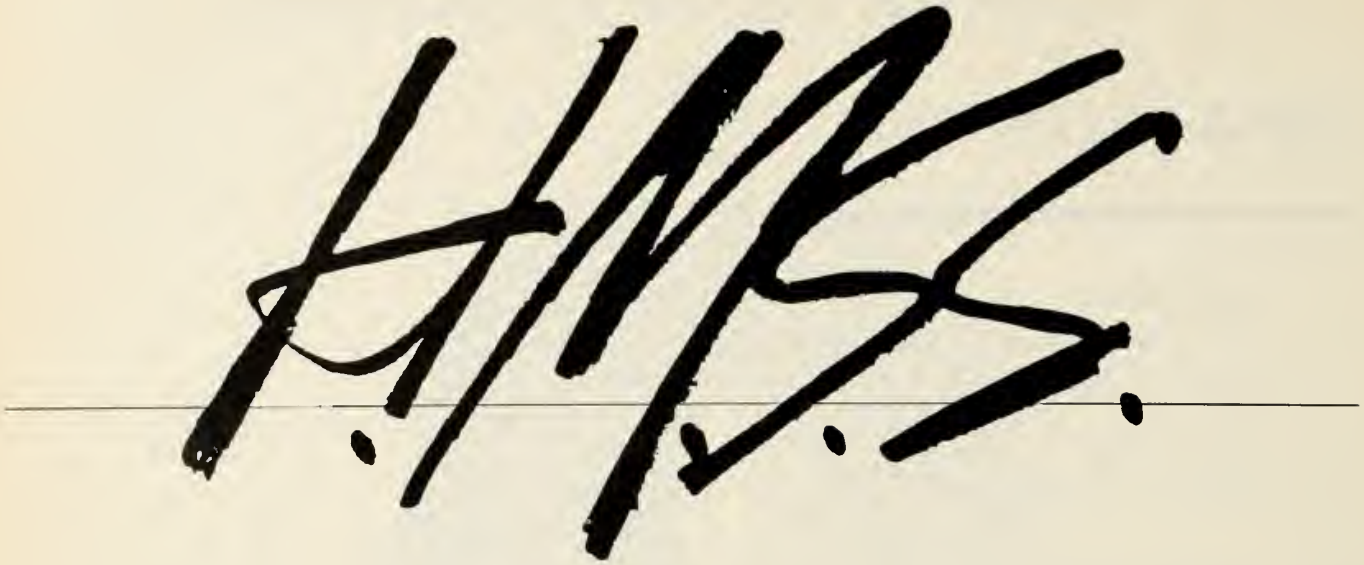
Norman D. Peters, MD

179 **Sixteen Years As Defense Committee Chairmanship**

Reminiscences of Beginnings of the Malpractice Crisis in Rhode Island

Francis B. Sargent, MD

COVER: *Photograph of Francis B. Sargent, MD provided courtesy of Mrs. Sargent.*



The AMA Hospital Medical Staff Section Ninth Assembly

JUNE 18-22, 1987 PALMER HOUSE CHICAGO

Represent your medical staff.

For Information Contact:

Department of Hospital Medical
Staff Services
American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610
Phone (312) 645-4747 or 645-4753

EDITORIAL

The Trials of Blue Cross and Blue Shield

Blue Cross and Blue Shield of Rhode Island has been much in the news of late. *The Providence Sunday Journal* of March 8, 1987 devoted two full pages to its recent trials and tribulations. Under the heading "Blue Cross fighting to keep its customers," it goes on to state that the "Traditional leader in health insurance faces competition from HMOs [and] others. These include commercial carriers. Fleet National Bank, Brown University, and the Providence Journal Co. are looking for alternatives because of major rate increases. Hasbro has already dropped out. HMOs have been taking away customers — the young and healthy according to Blue Cross. Last year alone 27,000 subscribers canceled Blue Cross coverage. Ocean State Physician Health Plan and Rhode Island Group Health Association (RIGHA) are the chief local competition. Metropolitan Life Insurance Co., Aetna, Allstate, and Connecticut General are actively entering the Rhode Island scene. Blue Cross President Douglas McIntosh's claim that the competitors are luring the young and healthy is disputed by the Rhode Island Health Department, according to a recent news report. We are not in a position to have an opinion on this, but the impact of competition cannot be denied. The Blues have endeavored to meet this challenge with its own HMO-Rhode Island. It is too early to judge the success of this new enterprise. A greater threat to the local Blues is a suit by Ocean State and the 325 member Physicians and Surgeons Association, a doctors union, for $60 million for alleged violation of federal and state antitrust laws. This is related to its "prudent buyer" policy, in which its proposes to reduce its fee payments to match a one-year withholding of 20 per cent of agreed fees by Ocean State due to fiscal constraints.

While these issues will be played out in the courts and the marketplace, a few observations may be in order about circumstances not always obvious to the casual bystander or even to the sophisticated reporter. McIntosh's assertion that Blue Cross-Blue Shield must inevitably be the best buy because it is a non-profit operation is probably correct in the long run and also consistent with the fact that historically it has always been a lean operation. But dollars and cents may not alone encompass the difficulties.

When Blue Cross started in 1939 with a few dozen employees it was a home-grown and accessible organization. Blue Shield, formed in the early post-war years, was similarly a small operation. Both have grown over the years together with increasing alienation from the hospitals and doctors, aggravated by the eventual divorce of the Blues respectively from the Hospital Association of Rhode Island and the Rhode Island Medical Society. The relationship has become increasingly adversarial. Later, the Blues became the carrier for federal Medicare Part A and the intermediary for Part B. The Blues eventually assumed management of the Delta Dental dental programs. Because of the inherent abrasions of federal regulations the unhappiness increased. Eventually they became the carrier, first for a three-state, and later for a vast regional area of CHAMPUS, medical care for the families of the armed forces. The organization, embracing all of these functions, now numbers an incredible 1500 employees, spread all over downtown Providence. These myriad activities have undoubtedly placed a severe strain on the administrative structure. Whether for subscriber, hospital, or other provider (physicians, dentists, laboratories, pharmacies), access to information or discussion of grievances can be a highly frustrating bureaucratic experience. Delays in payment of bills, sometimes unfairly attributed to the Blues, may be a result of federal administrative problems, but an explanation of the facts is not always sufficient. "I am sorry," or "we realize the difficulties" is seldom heard. A climate of arrogance or soulless bureaucracy is not helpful, whether dealing with subscribers or providers. The profit-making companies or other user-friendly competition are much better at this sort of thing. "Cute" advertisements for public relations purposes are in the long run more abrasive than helpful.

It is certainly too early to write the Blues off. Yet it would serve them well, in view of a number

of undoubted advantages which they enjoy, to improve their image, even to group buyers, through true kindness, accessibility, affability, and friendliness.

Seebert J. Goldowsky, MD

More On Tobacco

There have been recent developments in the war on smoking that a few years ago one would not have dreamed possible. Berkeley, California and Cambridge, Massachusetts, both university towns, have adopted highly restrictive ordinances limiting smoking in public places. Similar legislation became effective in New York state on May 7. On the local scene Rhode Island Hospital, the Rhode Island Health Department, and Blue Cross-Blue Shield of Rhode Island have at last adopted realistic non-smoking rules for their premises. The Rhode Island General Assembly, long a bastion of hold-outs, has now banned smoking in the Senate and House chambers. Several large corporations have banned smoking entirely on the premises. It became clear to several large companies that it was unfair to permit a person to smoke in a private office, usually someone in management, while a person in a typing pool could not. Incidentally, the Rhode Island Medical Society at its last House of Delegates meeting voted to make its entire headquarters building a non-smoking area.

Yet much remains to be done on both the local and national scenes. The restrictions on smoking in Rhode Island restaurants are inadequate and poorly enforced. Very few restaurants are properly posted with a sign indicating the availability of a no-smoking area as required by law, and fewer still bother to accomodate patrons voluntarily. A few even seem to resent the question, when asked. Considering that 70 per cent of the population are non-smokers, it is inequitable to provide much less than half of the space as a smoking area for this majority. Furthermore, in some cases the non-smoking tables are close to the kitchen, in a dark corner of the restaurant, or in a sort of Siberia. When non-smokers are treated as the favored customers, true equity will have been attained. Regulations regarding smoking in the workplace appear to be adequate if truly enforced. The distribution of free cigarette samples also should be banned.

It is hoped that one day soon Congress will have the courage to ban tobacco advertising and promotion. Large numbers of children, the target of the industry's seductive advertising, continue to take up the habit, even though some one thousand deaths each day are attributable to tobacco use. In this connection the sponsorship of sporting events by tobacco companies should be outlawed. Tobacco price support laws are also ridiculous in the face of the repeated warnings from a whole series of surgeons general, including the present incumbent. A total ban of smoking on domestic airlines is likewise overdue. The foul air in the half dozen or so rows in the rear of the plane allotted to smoking are still a nuisance to non-smokers who must pass through the area to reach rest rooms. Non-smoking flight attendants (although, alas! too few in number) must live and work in this foul environment, highly detrimental to their health. There also appears to be no assurance that this air is not recirculated in the rest of the cabin.

The tobacco industry, despite its bravado defense of smoking, obviously has grave concerns about the future. The take-over of General Foods by Philip Morris and Nabisco by R.J. Reynolds are certainly straws in the wind. It is ironical that these titans of tobacco are now touting the salubrious virtues of decaffeinated coffee and high-bran cereals. And now, the greatest irony of all, it is rumored on Wall Street that Philip Morris may eventually withdraw from the tobacco industry entirely.

Last but not least, it is sad that the Supreme Court in January let stand a lower court ruling that the health warnings on cigarette packages protected manufacturers from certain health-related lawsuits. Yet legal experts have pointed out that this does not necessarily establish a precedent for all future cases. Although the tobacco industry was ecstatic over this outcome, it is significant that over 200 such suits have been filed and some 145 are still pending. The Supreme Court still has the option of taking up some future case or cases directly. Where there is life there is hope. A ruling favorable to a plaintiff may still be possible and would be devastating to the industry.

Seebert J. Goldowsky, MD

Issues in the Management of Recurrent Headache

Non-Pharmacological Treatment Offers Relief to Many Victims

Virginia Attanasio, PhD
Joanne L. Fowler, PhD
Michael J. Follick, PhD
Richard J. Perry, MD

Although not a life-threatening disorder, headache is an extremely prevalent and costly health-care problem. Virtually everyone will experience headache at some point in his or her life, and recent evidence suggests that 50-70 per cent of all adults report at least one headache per month.[1-3] Further, 10-30 per cent of adults will experience frequent and severe headache which will significantly impair their functioning.

Perhaps because of the belief that headache is a benign problem, only 25 per cent of all headache sufferers seek medical treatment. Nonetheless, 42 million Americans consult a physician each year for a primary complaint of a headache.[1-4]Although medication is the primary method of treatment, less than 50 per cent of all patients treated report a reduction of their headache symptoms with pharmacological interventions. Despite this poor outcome, billions of dollars are spent each year on over-the-counter and prescription medications. A recent study of patients attending a headache-treatment clinic indicated that patients spent approximately $500-$1000 per year on their headache problem, *after* the cost of the initial diagnostic evaluations. The significance of this figure is apparent when considering that these headache patients, on average, had experienced headaches for 15 years prior to entering treatment.[1] In addition, headache is responsible for billions of dollars in lost work time each year. Consequently, when one considers the monetary cost of headache to patients, employers, and insurance carriers, the figures are staggering.

Virginia Attanasio, PhD, is a Post-Doctoral Fellow, Department of Psychiatry and Human Behavior, with the Brown University Program in Medicine.

Joanne L. Fowler, PhD, is Program Coordinator for The Miriam Hospital Headache Clinic and a Clinical Assistant Professor of Psychiatry and Human Behavior with the Brown University Program in Medicine.

Michael J. Follick, PhD, is Director of The Miriam Hospital Chronic Pain Treatment Program; and Associate Professor of Psychiatry and Human Behavior with the Brown University Program in Medicine.

Richard J. Perry, MD, is a Clinical Instructor of Medicine with the Brown University Program in Medicine. His hospital affiliations are The Miriam Hospital, Rhode Island Hospital, and Roger Williams General Hospital.

However, the magnitude of the headache problem far exceeds its monetary costs. In addition to the patients' pain and suffering, headache can produce marked lifestyle disruption, including impairment in marital and family relationships, educational and vocational difficulties, social and recreational disturbance, medication over-reliance, and emotional distress.

In recent years there has been an increasing awareness of the problem of chronic headache, which has prompted alternative conceptualizations of the problem, and the development of various treatments. Specialized headache clinics have been established for the delivery of these services. The purpose of this paper is to review briefly the classification of headache types, present a biopsychosocial conceptualization of the problem, and discuss treatment alternatives, including non-pharmacological interventions. Additionally the development of specialized headache clinics to deliver these services will be described, using The Miriam Hospital Headache Clinic as an example.

Classification of Headache

The most widely used classification of headache was developed by the Ad Hoc Committee on the Classification of Headache, and delineates 15 categories, based on phenomenology and etiology.[5] While in recent years various headache experts have developed other classification systems, the Ad Hoc Committee criteria nonetheless remain the standard for headache diagnosis.

Three of the fifteen identified categories account for more than 80 per cent of all headaches which present to health care providers. The primary features of these three headache types are presented in Table 1.

Medical Treatment

Traditionally, the most common treatment for headache is pharmacotherapy, whether self-administered over-the-counter preparations or physician prescribed agents. The use of medication is appealing primarily due to its relative ease and economy of administration. The types of medication strategies employed fall into three categories: abortive, designed to prevent the headache from completing its natural course; palliative, designed to decrease the intensity of symptoms, and prophylactic, designed to prevent the onset or reduce the frequency of episodes.

Of these, perhaps the most common is the use of palliative (or analgesic) agents, ranging from narcotics such as meperidine and oxycodone to non-narcotic over-the-counter preparations such as aspirin and acetaminophen. While analgesic preparations are effective for patients with infrequent acute headache, they are typically ineffective for patients with increasingly frequent and severe headache. Not surprisingly, this can lead to patients escalating dosages and developing problems with chemical tolerance and dependence.[6,7]

Table 1. — Diagnostic Criteria

Vascular Headache of the Migraine Type

Common Migraine Headache — (a) episodic, usually of 24-48 hour duration, which typically occur no more than once per week; (b) onset typically unilateral; (c) often accompanied by nausea and vomiting; (d) frequently described as pulsatile, and often located in the temporal or orbital areas; (e) sonophobia and/or photophobia during an episode; (f) onset and resolution typically abrupt; (g) family history of migraine.

Classical Migraine Headache — In addition to the above of common migraine; (h) prodromal symptom(s) which may include visual disturbances, speech disturbances and sensory-motor disturbances.

Cluster headache — (a) bouts of acute headache, separated by pain-free intervals ranging from weeks to years; (b) episodes are of brief duration (minutes to several hours) and are present at least every other day. Other common, but not necessary features include unilateral, stabbing pain and lacrimation, rhinorrhea, pupillary constriction, flushing, and diaphoresis.

Muscle Contraction Headache

(a) frequent episodes, usually occurring several times per week; (b) onset and resolution typically slow and gradual; (c) frequently begin in cervical, occipital or sub-occipital areas; (d) often described as a sensation of tightness or pressure, or a constant ache; (e) symptoms usually exacerbated by stress. Time course of symptoms is critical in diagnosis, as muscle contraction headache during the later stages may be experienced as pulsatile and accompanied by nausea, vomiting, photophobia and sonophobia.

Combined Headache: Vascular and Muscle Contraction

(a) meets some or all criteria for both migraine and muscle contraction.

Abortive agents are most commonly used with migrainous headache and include the various ergotamine and vasoconstrictive preparations. However, drugs such as sedatives and muscle relaxants also are used abortively in the treatment of muscle contraction headache, based on the rationale that they affect the underlying pathophysiology of the headaches.

The use of prophylactic agents is less common and is usually reserved for patients with very frequent and severe headache, such as those experiencing headache several times a week. Types of drugs used for prophylaxis vary widely, but

commonly include ergotamine and ergot derivatives, non-steroidal anti-inflammatory agents, cardiovascular agents such as beta and calcium channel blockers, tricyclic antidepressants, minor tranquilizers, muscle relaxants, and sedative-hypnotics. Additionally, some evidence suggests that antihistamines, phenothiazines, and lithium carbonate have also been effective in individual cases.

As previously mentioned pharmacotherapy is increasingly ineffective as headache becomes chronic and often leads to habituation, dependence, and escalating medication use. Of additional concern is recent evidence which suggests that regular and frequent use of both analgesics and vasoconstrictive agents may actually lead to the maintenance and exacerbation of headache, frequently termed "rebound headache." The dosages suspected of producing this phenomenon are relatively low, with approximately 14 (325 mg) tablets of aspirin or its equivalent, or 4-5 mg of ergotomine per week being sufficient.[8,9]

In addition to its potential for developing dependence and exacerbating headache, medication also has other limitations. First, even relatively benign drugs such as aspirin or acetaminophen, when used frequently over extended periods, can produce harmful side effects, and even toxicity. It is notable that the toxic range for many analgesics, including aspirin and acetaminophen, is not particularly high. This has potential implications for patients with chronic headache who may consume as many as 20-30 tablets per day, 2.5-3 times the maximum daily recommended dosage. Second, many drugs, such as the tricyclic anti-depressants, can produce uncomfortable side effects; and others, like the narcotics and tranquilizers, can interfere with normal performance and functioning.

A Biopsychosocial Conceptualization

One recent hypothesis that has been proposed to account for the relatively poor response of chronic headache to traditional treatment suggests that these interventions fail to consider the multi-faceted dimensions of the problem. Headache was conceptualized and treated as if the primary mechanism was either biological or psychological. Consequently, treatment was either pharmacological (eg, vasoactive, muscle relaxants, analgesics), or when medication failed, psychological (eg, traditional psychotherapy or psychopharmacotherapy). Not surprisingly, neither of these unilateral treatment approaches has met with significant success. In recent years, emphasis has instead been placed on the interrelationship of stress and psychophysiological variables, and headache is increasingly being considered a complex pain problem, rather than a specific unique physiological disorder.

This has led to the development of a model which integrates the various biological, psychological, and social dimensions of a chronic headache problem. This model proposes that the biological changes which occur during a headache may be triggered through a number of biological and psychological factors, which operate through the autonomic nervous and endocrine systems. While initially these triggers may be in any one sphere of functioning (ie, biological, psychological, social), it is likely that as the headache problem progresses all three spheres become involved. Thus, headache may be triggered by biological factors including menstrual cycle changes, hormonal medications, and foods such as chocolate, aged cheese, and alcohol; psychological factors such as fatigue, anxiety, and depression; and social stresses such as divorce, job difficulties and financial problems. Additionally, once the headache occurs, it may itself become a stressor, and thus serve to further perpetuate the headache problem.[10,11]

The cyclic interactive nature of this model clearly elucidates why interventions aimed at only one aspect of the problem are frequently ineffective. This biopsychosocial model proposes that treatment needs to be multi-dimensional in order to address the various components of the problem.

A number of alternative treatments have been developed from this model. The three most common interventions include relaxation training, biofeedback, and cognitive therapy (eg, coping skills training) in conjunction with psychotherapy. While these procedures are typically effective when used alone, most often patients are trained in more than one procedure in order to maximize treatment outcome. The types of treatments used depend on the individual patient's presenting symptoms. Although differing slightly in technique, the goal of these procedures essentially is to teach patients physiological and psychological self-control. Once patients have learned these skills, they can intervene in the headache cycle both by producing physiological changes which affect headache activity and coping more effectively with various stresses that both precipitate and perpetuate the headache problem.

Non-Pharmacological Intervention Strategies

Relaxation Training. While this procedure may be taught in several ways, essentially all are designed to produce deep levels of muscle relaxation, lowered autonomic arousal, and subjective feelings of relaxation. The techniques employed may include passive meditation, diaphragmatic breathing exercises, visual imagery, or a more structured procedure known as progressive relaxation, which utilizes specific tension-release cycles of muscle groups throughout the body. There are multiple variants of progressive relaxation, however, most represent modifications of the original procedure developed by Jacobson.[12] In the treatment of headache, this intervention is useful in reducing the cumulative physical build-up from daily stress and in modifying problematic physiological arousal. Although relaxation training is taught in a series of sessions, as with any skill it requires that patients practice the techniques regularly so that they can maintain the skill and effectively employ it in their home and work environments.

Biofeedback. Similar to relaxation training, biofeedback is designed to teach patients self-control over specific physiological functions, including responses of the autonomic nervous system and the musculoskeletal system. The rationale for treatment is the specific physiological responses believed to be involved in the etiology and maintenance of a particular headache type (ie, muscle tension levels for muscle contraction headache, peripheral temperature and cephalic vasomotor activity for migrainous headache).

Biofeedback applications developed from early work in the classical and operant conditioning of physiological responses, and have been widely used in the treatment of psychophysiological or stress-related disorders. In particular, biofeedback has been widely used in the treatment of headache, and there is a vast body of literature documenting its efficacy.

As previously mentioned, biofeedback and relaxation training are similar in their end goals, namely producing voluntary control over physiological responses, including lowering of autonomic arousal. However, the two differ in the method by which these changes are produced. Whereas relaxation focuses primarily on feelings of general relaxation which are secondarily accompanied by specific physiological changes, biofeedback attempts to produce directly the specific physiological change which secondarily may be accompanied by feelings of relaxation. This procedure is accomplished by instrumentation which monitors the physiological response of interest, and then provides the patient with "feedback" regarding the direction and magnitude of any changes. Consequently, the patient has almost immediate information regarding the effect of various strategies utilized to produce change. Once a patient demonstrates control of a response, the use of external feedback is faded. This serves to decrease the patient's dependence on the external feedback, and facilitates the generalization of skills to settings outside the therapy sessions.

Cognitive Coping Skills. In addition to physiological changes, patient's cognitions or subjective experiences of stresses also play a role in the development of maintenance of a recurrent headache problem. A patient's inability to cope effectively with stresses can prescipitate and maintain a headache. Furthermore, an often unrecognized stressor is the headache itself.

The most common model of cognitive coping skills was developed by Holroyd and Andrasik, who identify several maladaptive cognitive responses which can mediate headache.[13] Over the course of treatment patients are taught to become increasingly aware of their life stresses and their cognitions and coping styles in response to these stresses. They are then taught several techniques systematically to modify these maladaptive patterns.

Treatment Outcome

The efficacy of the above non-pharmacological treatment interventions has been widely investigated over the past 15 years. The results suggest that these treatments represent viable alternatives for patients with chronic headache problems.[1, 14, 15]

Overall research indicates that biofeedback, relaxation, and cognitive coping techniques are highly effective when used both alone and in various combinations, and significantly more effective than either pharmacotherapy or psychotherapy alone. Averaging the results of the numerous outcome studies examining these techniques, it appears that 60-70 per cent of all migrainous headache patients and 50-65 per cent of all muscle contraction headache patients experienced better than a 60 per cent reduction in headache symptoms with non-pharmacological treatments.[1]

Not surprisingly, there are individual differences in patients' response to these various treatments, and thus patient-treatment matching is critical. Comprehensive evaluation is essential

since non-pharmacological treatments are not effective for all types of headache problems or for all patients. Although psychiatric difficulties, such as mild to moderate depression, anxiety, and somatization, do not preclude non-pharmacological treatments, patients exhibiting major or primary psychiatric disorders are less likely to benefit. Headaches most likely to respond to these treatments are classical and common migraine, muscle contraction headache, and combined migraine and muscle contraction headache. Patients with other headache types, including cluster headache, "menstrual" migraine, and posttraumatic headache, are less likely to exhibit clinically meaningful improvement. Patients with episodic headache, as opposed to continuous headache, are also more likely to respond to these treatments. However, recent evidence suggests that medication withdrawal in conjunction with non-pharmacological treatments may be effective for patients with continuous headache, and we are currently undertaking a systematic investigation of these procedures at The Miriam Hospital Headache Clinic.

Headache Clinics

Headache clinics have become the primary mode of delivering alternative treatment strategies. Some clinics offer both medical diagnostic services and comprehensive treatment programs. Other clinics are primarily treatment oriented and work closely with referring physicians who have performed thorough medical evaluations, and often initiated minimally successful treatments. These clinics are usually outpatient based programs offering a wide range of non-pharmacological treatment strategies. The Miriam Hospital Headache Clinic is a typical example of such a treatment oriented clinic.

The goals of the program are: (1) to reduce the patient's headache activity as measured by the frequency, duration, and intensity of headache; (2) to improve the patient's ability to cope with their headache problem; (3) to eliminate the patient's reliance on medications; (4) to educate the patient about the disorder of headache; and (5) to reduce over-utilization of the health care system. The treatment strategies offered include all the major non-pharmacological interventions: relaxation training, biofeedback, cognitive therapy and psychotherapy.

The first contact the patient has with the clinic is a comprehensive evaluation to determine which, if any, of the available treatment strategies are likely to be beneficial. One factor involved in determining appropriateness is diagnostic impression, since not all headaches respond to these types of treatment. In addition, patients must be willing to adopt a self-control approach to their headache problem, where they are active participants in their treatment rather than passive recipients. They must also, with their physician's approval, be receptive to reducing or eliminating their use of headache medications.

At the conclusion of the evaluation, the biopsychosocial model of headache is presented, and treatment options are discussed with the patient. If the patients have not been medically evaluated prior to their initial contact with the clinic, appropriate referrals will be made. Patients who elect to enter treatment are scheduled for weekly appointments at which various non-pharmacological treatments are tailored to their individual needs. Emphasis is placed on home practice in order to facilitate the integration of treatment gains into their lifestyles. Treatment is short term and goal-oriented, lasting approximately eight to fifteen weeks. Follow-up sessions are scheduled as necessary, and the patient's referring physician is kept apprised of the patient's progress.

Conclusion

Headache is an extremely prevalent and costly disorder. While medication can be effective in managing acute intermittent headache problems, it is often ineffective for increasingly chronic headache. Non-pharmacological treatments are a useful alternative for many of these patients, frequently resulting in substantial improvements in their headaches and lifestyle disruption. The program at The Miriam Hospital is a specialized clinic offering comprehensive evaluations of the problem, as well as non-pharmacological treatments for appropriate patients.

References

1 Blanchard EB, Andrasik F: Management of Chronic Headache: A Psychological Approach. New York, Pergamon Press, 1985.

2 DeLozier JE, Gagnon RO: National ambulatory medical care survey: 1973 summary, United States, May 1973-April, 1974. DHEW Publication No. 76-1772. Washington, DC: U.S. Government Printing Office, 1975.

3 Attanasio V, Andrasik F: An examination of headache in college students: Headache, in press.

4 Waters WE: Community studies on prevalence of headache. Headache 9:298-307, 1970.

5 Ad Hoc Committee on the Classification of Headache: Classification of Headache. Journal of the American Medical Association 179:717-718, 1962.

(Continued on page 170)

There are three ways to bill

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85		Medicare pmt/adj.		-45.-	-8.-	47.-
10/10/85		patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		Pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/Adj		-25.-	-5.-	807.-
1/17/86		Court adj.			-3.-	804.-
2/2/86		Medicare pmt/Adj		440.-	250.-	114.-

PLEASE PAY FROM THIS STATEMENT

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS YOUR ACCOUNT AS APPEARS ON YOUR EDITH ARC

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86 DATE 2/21/86
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

our patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Words are *printed*. You're not judged by someone else's scribbles.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

Patient year-to-date payment totals.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A

STATEMENT

FED I.D. #DD-D000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG. CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	L O	DESCRIPTION	CHARGES PAYMENTS ADJ. PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS	NEW BALANCE	PATIENT	INSURANCE
.00	4.00	.00	.00	.00		4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT" NEW BALANCE" SHOWN.

STATEMENT DATE	PATIENT PAY Y.T.D.	ACCOUNT NUMBER
02/21/86	.00	12090

LOCATION CODES
1 OFFICE 2 HOSPITAL IN PATIENT 3 HOSPITAL OUT PATIENT 4 OTHER 5 OTHER 6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

[6] Peters BH, Fraim CJ, Masel BE: Comparison of 650 mg aspirin and 1,000 mg acetaminophen with each other, and with placebo in moderately severe headache. The American Journal of Medicine:36-42, June, 1983.
[7] Warner G, Lance JW: Relaxation therapy in migraine and chronic tension headache. The Medical Journal of Australia 1:298-307, 1975.
[8] Saper JR: Headache Disorders: Current Concepts and Treatment Strategies. Boston: John Wright — PSG Inc, 1983.
[9] Kudrow L: Paradoxical effects of frequent analgesic use. Advances in Neurology 33:335-341, 1982.
[10] Bakal DA: A biopsychological perspective. Psychological Bulletin 82:369-382, 1975.
[11] Holroyd KA, Andrasik F: Do effects of cognitive therapy endure? A two year follow-up of tension headache sufferers treated with cognitive therapy or biofeedback. Cognitive Therapy and Research 6:325-334, 1982.
[12] Jacobson E: Progressive Relaxation. Chicago: University of Chicago Press. 1938.
[13] Holroyd KA, Andrasik F, Westbrook T: Cognitive control of headache. Cognitive Therapy and Research 1:121-133, 1977.
[14] Adams HE, Feuerstein M, Fowler JL: Migraine headache: Review of parameters, etiology and intervention. Psychological Bulletin 87:217-237.
[15] Attanasio V, Andrasik F, Blanchard EB: Cognitive therapy and relaxation training in the treatment of muscle contraction headache: An examination of efficacy and cost-effectiveness. Under review.

164 Summit Avenue
Providence, RI 02906

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY....ANYWHERE

PLUS insurance for....
tax audit
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

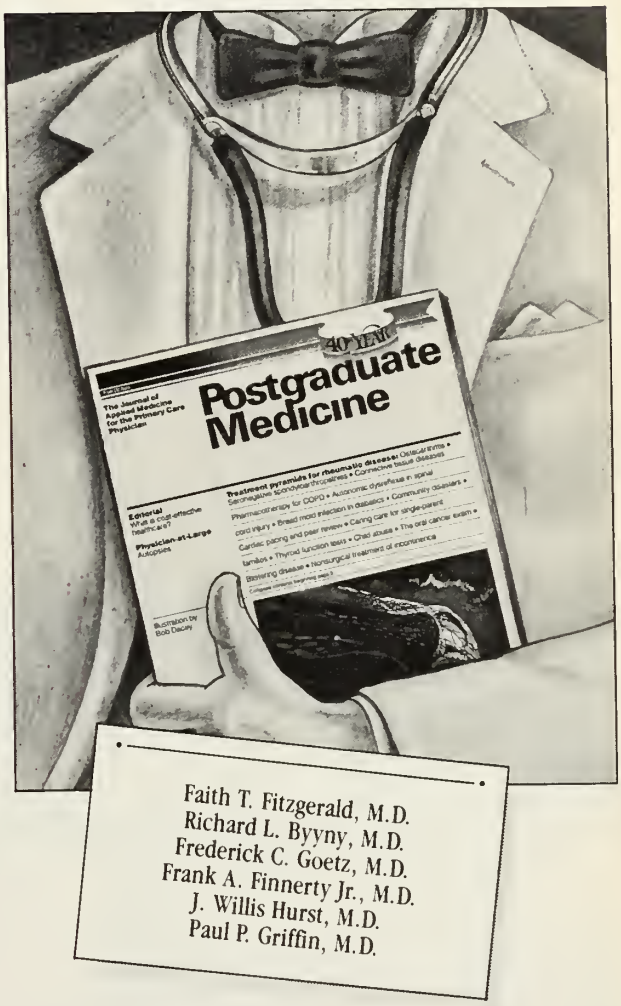
Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

FAMOUS PHYSICIANS ARE SHOWING UP FOR OUR 40th YEAR CELEBRATION.



Read Every Issue From Cover to Cover:

April
Symposium: Focus on General Internal Medicine ..... Faith T. Fitzgerald, M.D. coordinator
Special Article: General Internal Medicine 1947-1987 ..... Richard L. Byyny, M.D.

May 1
Symposium: Diabetes Mellitus
Special Article: Diabetes Mellitus 1947-1987 ..... Frederick C. Goetz, M.D.

May 15
Symposium: Hypertension ..... Frank A. Finnerty, Jr. coordinator
Special Article: Cardiology 1947-1987 ..... J. Willis Hurst, M.D.

June
Symposium: Orthopedics in Primary Care
Special Article: Orthopedics 1947-1987 ..... Paul P. Griffin, M.D.

40 YEAR
Postgraduate Medicine

Every Issue is a Celebration of Clinical Information

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

Chordomas: A Review

Early Diagnosis and Complete Removal Offer Potential for Cure

Norman D. Peters, MD

Chordoma is a histologically benign tumor which originates from the intraosseus notochordal remnants.[1,2] The rest of the primitive notochord ordinarily will appear in the fourth week of embryonic life and generally regress by the seventh week. In the adult, only the centrum of the nucleus pulposus is a derivative of this primitive structure. Notochordal vestiges may be found embedded in the dorsum sellae in 4 to 5 per cent of adults, and ectopic notochordal tissue may even be seen loosely attached to the ventral surface of the brain stem. This, however, is of little or no pathologic significance.[2] This midline congenital lesion comprises 3 to 4 per cent of primary brain tumors and accounts for about 38 per cent of presacral tumors.[3] Fifty per cent of all chordomas occur in the sacrococcygeal area with 35 per cent occurring in the skull base and another 15 per cent in the vertebral bodies.[3,5] Grossly, the tumor appears as a glistening lesion with a smooth pseudocapsule. The cut surface varies from soft to firm and may be gray to opalescent in color. Microscopically one sees a compact mass of elongated cords of physaliphorous, or clear cells with a vacuolated cytoplasm. One may see fibrous septa, and there is generally a mucopolysaccharide stroma. Mitotic figures are extremely rare, and the overall appearance is one of a relatively benign lesion.

Norman D. Peters, MD is Attending Surgeon at The Miriam Hospital; Consulting Neurosurgeon at the VA Hospital; Director of the Division of Neurosurgery at Roger Williams General Hospital; and Clinical Assistant Professor of Neurosurgery, Brown University.

The typical radiographic findings of sacral chordomas are those of destruction of the sacral segments by an expansile ballooning mass (fig 1a, 1b). There tends to be a prevertebral soft tissue mass. Lesions in the skull base show the same destructive potential in the clivus that the sacral lesions display. Sacral lesions on x-ray examination and on computed tomography (CT) scans reveal well-circumscribed, rather homogenous lesions in the presacral area (fig 2a, 2b). Lesions in the skull base tend to expand intracranially and to destroy surrounding bone. Forty to fifty per cent of these lesions will have calcification.

Chordomas present a treatment spectrum of incurable to completely curable lesion. Because of the extensive skull base destruction and dural and intradural involvement with major intracranial vascular and neural structures, the skull base lesions tend to be an incurable entity at this time (fig 3). The presacral or retrorectal chordoma, because of its isolated position, has the potential for complete cure. Probably a reason for the massive size and destructive capability of these tumors is the fact that they tend to be diagnosed late. Skull base lesions are diagnosed usually when cranial nerve findings or other neurologic sequelae occur.

The pelvic lesions, if not diagnosed on careful routine rectal examination, will begin to show symptoms when the patient develops cauda equina or sacral nerve root dysfunction as well as low back pain. The presacral chordoma lies in the retrorectal space, which is a potential space lying anterior to the sacrum and coccyx and posterior to the rectum.[3,4] This space is bounded

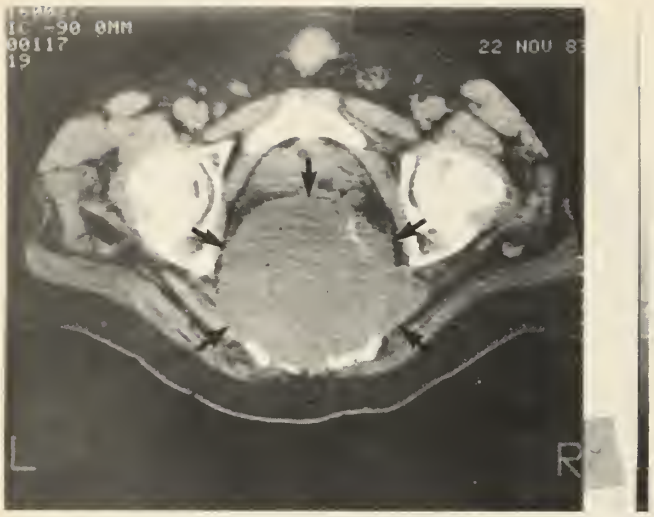


Fig 1a. Pre-operative CT scan of a large chordoma filling retrorectal space and destroying mid and lower sacrum (black arrows outline lesion).

Fig 1b. Same tumor as in 1a showing destruction of lower sacrum and coccyx.

inferiorly by the levator ani and the coccygeal muscles. It is bounded superiorly by the pelvic peritoneal reflection and laterally by the ureters and the iliac vessels. The treatment of sacral chordoma is that of *en bloc* sacral amputation.[3-7] This technique was first described by Stenner and Gunterberg in 1978.[6] What is of importance here is that the sacral periosteum and the presacral fascia elevate along with the tumor and act as a fairly strong unbroken anatomic barrier to tumor growth. Therefore the rectum and other organs are displaced, but are not infiltrated by tumor. It is therefore a mistake to do a transrectal biopsy for spillage of tumor into the peritoneum will cause metastatic implants.

It has been our finding, as well as that of others, that when the sacrum is to be amputated for cancer, one must include at least one vertebra proximal to the radiographic limit of the tumor.[6] If, on x-ray examination, the tumor has broken through up to but not beyond the disc space between S2 and S3, it may be possible to preserve the S1 root. If S2 is completely involved with chordoma, amputation above the S1 canals is indicated.

Small tumors in the range of 4 cm in diameter can be easily removed via a posterior approach involving osteotomy of and amputation of the lower sacrococcygeal component (fig 2c). For larger tumors which are filling the pelvis, our technique has been that of a combined abdominal-sacral approach.[7] For this approach, the patient is placed in a lateral decubitus position where the entire abdominal area and lumbosacral region are prepared. The general surgical and neurosurgical teams work simultaneously. While the neurosurgeon is widely exposing the lumbo-sacral-coccygeal region, the general surgical team is performing a standard laparotomy with mobilization of the rectum, identification of the ureters, and ligation and division of the internal iliac arteries. The prevertebral fascia down to the tumor is dissected off of the sacrum. When the sacral bone is visualized, a series of Steinmann pins are passed through the sacrum in an anterior to posterior manner to give an indication of where the

Fig 1c. Postoperative scan (3 years) showing complete removal of tumor and

sacral amputation need be carried out. This technique was devised by Doctor Stanley Simon. One must keep in mind that the sacral roots originate from the cauda equina and pass from the posterior to the anterior sacral holes in an oblique fashion. Once the determination of the level of amputation has been carried out, the neurosurgical team unroofs the part of the sacrum to be excised and judiciously ligates and divides the sacral roots in the canal. Next a series of osteotomes and punches are used to carry the amputation out into the ilium. Both teams work to mobilize the entire sacrum with tumor and involved nerve roots in an en bloc fashion (fig 1c). Again, care must be taken not to spill tumor contents into the pelvis.

For lesions that are unresectable in the skull base or are partially removed from the sacrum, the only present adjunct to surgical treatment is high-dose radiation therapy. In a long-term study of radiation therapy of these lesions at the Massachusetts General Hospital,[8] it was concluded that no discernable difference in "palliation" is achieved between patients with radiation therapy (less than 60 GY) and pure biopsy. All patients treated with radiation therapy regardless of the

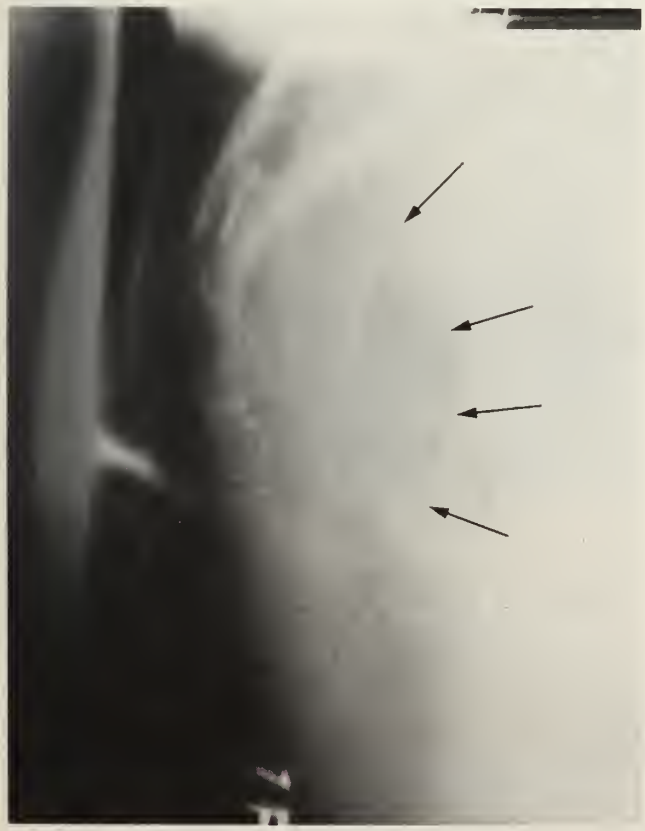
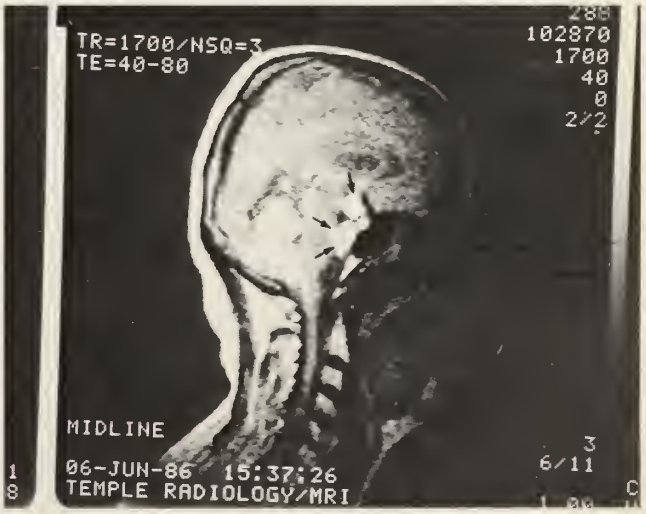


Fig 2a. Pre-sacral soft tissue mass (arrows).

Fig 2b. Pre-operative CT scan revealing small (4cm) sacrococcygeal chordoma.

Fig 2c. Postoperative scan showing complete removal of tumor pictured in 2b.

Fig 3. Magnetic resonance scan depicting a large intradural chordoma. Arrows outline tumor and extent of displacement of entire brainstem.



extent of their surgery, who are relatively free of disease progression, receive greater than 60 GY. This is carried out with a combination of proton-photon-beam treatment. With the use of proton beams and the Bragg peak technique of radiation therapy, ion beams can penetrate a definite controllable distance and can be made to stop within a designated, and very often small tumor area. By placing the Bragg peak on the tumor, one achieves a very rapid buildup in dose within the tumor, while a very low dose is given to the skin and surrounding tissues. One may give doses as high as 70 to 80.5 GY within a 2 to 3 mm distance of the brain stem. This type of treatment has lent itself very well to the treatment of fairly small circumscribed lesions in the skull base or even in the vertebral body.[9, 10]

The chordoma which represents the largest number of congenital retrorectal and skull base tumors still remains a treatment enigma. The tumor is histologically benign but because of delayed diagnosis and expansile growth very often is allowed to do excessive destruction and reach what was thought, in the past to be insurmountable size. Sacral lesions, even if they reach large size, carry the potential for complete removal and cure. Lesions found in the skull base and intracranial compartments do not carry such a happy prognosis. Very high dose, precisely focused radiation therapy has been of great value and has given us some degree of hope in dealing with surgically unresectable lesions. Early diagnosis, however, still offers the best possibility of achieving cures of these lesions.

References

1. Rich TA, Schiller A, Suit HD, Maukin HJ. Clinical and Pathologic Review of 48 Cases of Chordoma. *Cancer* 56:182-187, 1985.
2. Rubinstein LJ. *Tumors of the Central Nervous System.* Armed Forces Institute of Pathology. 1972, pp 315-318.
3. Mindell RD, Current Concepts Review — Chordoma. *Journal of Bone and Joint Surgery* 63-A, No. 3, March 1981.
4. Joa S, Beart RW, Spencer RJ, Reiman JM, Ilstrup DH. Retrorectal Tumors — Mayo Clinical Experience. 1960-1979. *Dis Colon Rectum* 1985, 28:644-652.
5. Sunderson N. Chordomas. *Clin. Orthopedics and Related Research.* No. 204, March 1986.
6. Stener B, Gunterberg B. High Amputation of the Sacrum for Extirpation of Tumors. *Spine* 3: No. 4; December 1978.
7. Huth JF, Dawson EG, Elber FR. Abdominosacral Resection for Malignant Tumors of the Sacrum. *Amer. Journal of Surgery* 148:157-161, July 1984.
8. Suit HD, et al. Definitive Radiation Therapy for Chordoma and Chondrosarcoma of base of skull and cervical spine. *J. Neurosurg* 56:377-385, 1982.
9. Saunders WM et al. Early Results of Ion Beam Radiation Therapy for Sacral Chordoma. *J. Neurosurg* 64:243-247, 1986.
10. Saunders WM, et al. Precision, High Dose Radiotherapy II. Helium Ion Treatment of Tumors Adjacent to Critical Central Nervous System Structures. *J. Radiation Oncol. Biol. Phys.* 11:1339-1347, 1985.

HMO RHODE ISLAND
MEDICAL DIRECTOR

HMO Rhode Island, Inc., a state licensed, federally qualified health maintenance organization, seeks a part time (50%) Medical Director. Candidates should be Board certified in one of the primary care specialties and have the demonstrated leadership qualities and administrative abilities necessary to serve as the Chief Medical Officer of a growing prepaid health plan.

Competitive reimbursement and fringe benefits.

Please forward C.V. prior to May 15, 1987 to Medical Director Search Committee, HMO Rhode Island, Inc., 30 Chestnut Street, Providence, R.I. 02903 or contact Michael Gerhardt at (401)274-6674 for additional details.

An Equal Opportunity Employer

HMO RHODE ISLAND
The Ultimate Health Maintenance Organization

A Nursing Home
Striving to Provide
The Ultimate in Nursing Home
Service

100 Wampanoag Trail *East Providence*
401/438-4275

Tenth Annual Seminar

CURRENT CONCEPTS IN FETAL AND NEONATAL CARE

May 28-29, 1987
Sheraton Islander
Newport, Rhode Island

Sponsors:

Rhode Island Medical Society
RI Chapter, American Academy of Pediatrics
RI Section, American College of Obstetricians and Gynecologists
RI Section, Nurses Section of ACOG
Women & Infants' Hospital
Brown University
RI Department of Health

Guest Faculty:

Loretta P. Finnegan, MD
John F. Huddleston, MD
Frank A. Manning, MD
Paula Meier, RN, DNSc

Faculty:

Elaine S. Barefield, MD
Lorand R. Brown, MD
Marshall W. Carpenter, MD
Patrice M. DiMario, RN, BS
Bente E. Hoegsberg, MD
Barry M. Lester, PhD
Anthony L. Mansell, MD
Betty R. Vohr, MD

Call 401/331-3207 for additional information

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

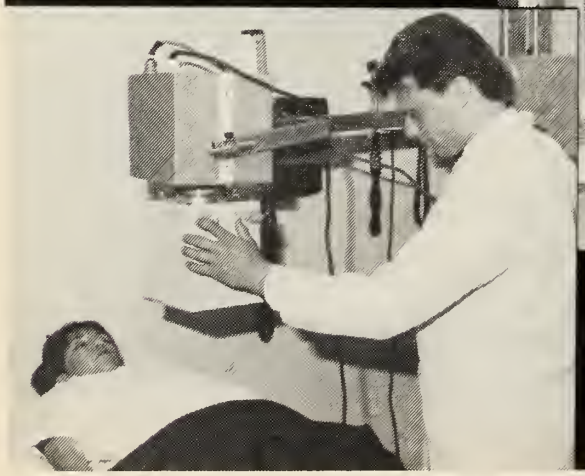
We've become the largest full service medical lab in Rhode Island...*because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Sixteen Years As Defense Committee Chairmanship

Reminiscences of Beginnings of the Malpractice Crisis in Rhode Island

Francis B. Sargent, MD

In 1953 the impossible happened. An otologist in Rhode Island, who had caused a facial paralysis, was sued by the patient, and a local otologist testified for the plaintiff. The award was $25,000. Insurance companies were very disturbed. They had expected doctors to protect each other. Some insurers withdrew from writing malpractice insurance. Others became very selective. The chairman of the defense committee of the Rhode Island Medical Society resigned. Doctor Earl Kelly, president of the Medical Society, and John E. Farrell, the Society's executive secretary, asked me to take over.

The first problem was to find a company that would write group insurance. We found a company that would insure doctors recommended by the committee and would not cancel out individuals, but it reserved the right to cancel the group.

Francis B. Sargent, MD is a Past President of the Rhode Island Medical Society; Consulting Otorhinolaryngologist, and Former Chief of The Department, Rhode Island Hospital.

Doctor Sargent recently retired from practice in his 94th year. He complained that his malpractice insurance premiums were getting out of hand. The name of his committee was later changed to the Mediation Committee.

It was obvious from the start that the company did not expect losses. Numerous complaints were taken care of, but finally the inevitable happened. An obstetrician faced with a floating fetal head pulled the patient's urethra off the bladder. A healthy child was finally delivered. The doctor foolishly admitted that this was the first time he had used Keeland forceps.

At the trial the patient's lawyer stated that his client was using Kotex sanitary napkins by the carload. On the second day of the trial, the defense lawyer approached me in the rear of the courtroom and said: "I can settle this for about $40,000," I said: "Better do it." There were four women on the jury who did not look friendly. Of course, the company cancelled the group.

With the help of Starkweather and Shepley insurance brokers, we found a replacement, the St. Paul Company. They agreed to write group insurance with the right to cancel individuals, but not the group. During the next eleven years our relations with St. Paul were very satisfactory. The defense committee reviewed 424 complaints. Ninety-two per cent were related to fees of $10-15 ($30 to $45 in 1986 money). Five per cent alleged discourteous treatment or neglect. Three per cent were more serious.

We were sharply criticized by Selig Greenberg, *Providence Journal* reporter for not keeping up with the progress in medicine. Some of the criticism was justified. We had two very bad "accidents." In one case a seven-year-old girl was

changed into a vegetable through a mixup in anesthesia. Anesthesia departments were booking more cases for a certain hour than they had doctors, depending on nurse "sitters" to care for excess cases. St. Paul hastened to settle this for $70,000.

In another instance a general practitioner doing obstetrics delivered a woman in one hospital, left her bleeding, and hastened to another delivery in another hospital. When he returned, the first patient had bled to death. Luckily St. Paul was able to settle this one for $8,000.00.

During the nineteen sixties the malpractice problem worsened. Attorney Melvin Belli in California had secured a verdict of $750,000 in a case where the surgeon had killed Jeff Chandler, a prominent movie actor. He had punctured the patient's aorta in an intervertebra disc operation.

At a national medical-legal meeting, Belli told us: "If you went into the operating room for a hernia operation and woke up with one eye out, you would see things differently."

The late Lawrence (Larry) Spitz, delegated by the AFL-CIO to establish a labor union-controlled HMO in Providence, published in the *Providence Journal* "30 cases of cheating by doctors," poorly documented. I was able to identify one. A neurosurgeon had sat up half the night waiting to see if a skull fracture would require decompression. Blue Shield allowed him a small fee. Thanks to Larry, we made the papers in Kiev, Russia as follows: "In the Province of Rhode Island in the United States of America, doctors are so dishonest that they are paid not to operate."

As the number of malpractice cases grew, our liability premiums increased. In 1970, when I resigned as the chairman of the committee, my surgical liability premium for $100,000-300,000 coverage had risen to $392. Physicians who did not operate were paying $80-100 a year.

By 1975 my premiums had risen to $1100. In desperation St. Paul agreed to issue *only* "claims made" policies. The Medical Society objected to this, and the *doctors* actually cancelled the no-cancellation agreement with St. Paul.

311 Hope Road
Cranston, RI 02920

THE DEPARTMENT OF ORTHOPAEDICS
AND REHABILITATION
RHODE ISLAND HOSPITAL
PRESENTS

THE SEVENTH ANNUAL KENNETH G. BURTON LECTURE

RICHARD G. EATON, M.D.
CLINICAL PROFESSOR OF ORTHOPAEDIC SURGERY
COLUMBIA COLLEGE OF PHYSICIANS AND SURGEONS
CHIEF, HAND SERVICE
ST. LUKE'S — ROOSEVELT HOSPITAL
NEW YORK, NEW YORK

"INTERPOSITION TENDON GRAFTS FOR CARPAL BONE REPLACEMENT"

"AN APPROACH TO THE TREATMENT OF ALL STAGES OF BASAL JOINT DISEASE"

FRIDAY, MAY 15, 1987
8:00 A.M.
GEORGE AUDITORIUM
RHODE ISLAND HOSPITAL

DEPARTMENT OF ORTHOPAEDICS
BROWN UNIVERSITY PROGRAM IN MEDICINE

LAW OFFICE OF HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

BOOK REVIEW

Psychiatry

Stanley Cobb, **A Builder of the Modern Neurosciences.** By Benjamin V. White, MD. Boston: The Francis A. Countway Library of Medicine, 445 pp, 1984.

Doctor Benjamin V. White has written a warm and vibrant story of the growth and development of a remarkable doctor, researcher, and teacher whose former students are scattered not only throughout the country, but also around the world. Since the Cobb papers were not available when White set out to gather his background information, he interviewed many family members, friends, colleagues, and former students.

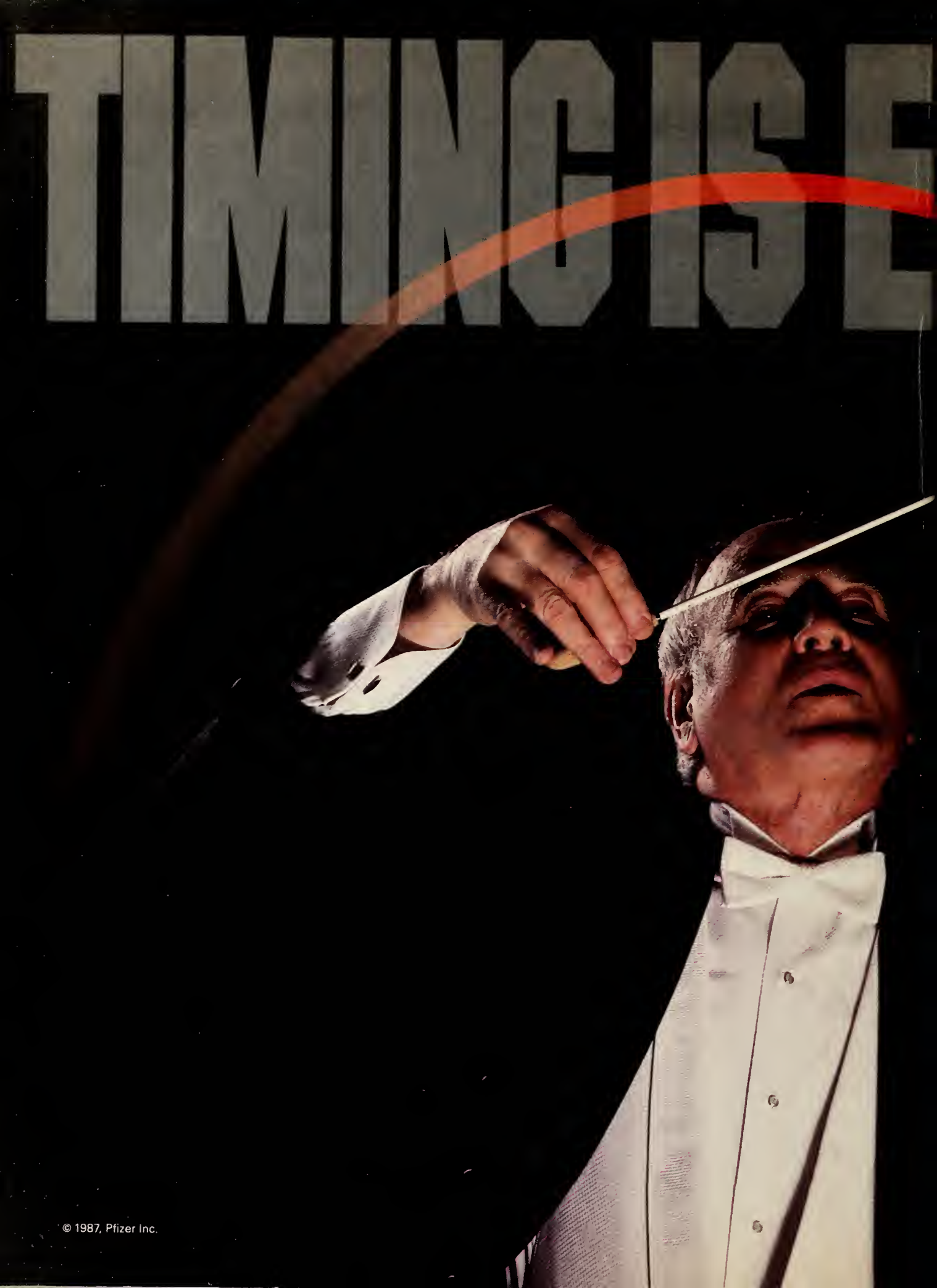
Cobb's childhood was spent in Brookline, Massachusetts near Jamaica Pond. While growing up there he developed a lifelong interest in nature, wildlife, and orinthology. He studied art when he was still a youngster, and painting was a great source of relaxation and satisfaction throughout his life.

While he was in medical school Doctor David L. Edsall, Cobb's professor of medicine at Harvard, recognized his potential and became his mentor for many years. It was at Edsall's suggestion that Cobb interned in surgery with Harvey Cushing, then went to Johns Hopkins to study psychiatry and neuroanatomy with Adolph Meyer and neurophysiology with William Howell. When he returned to Boston he went to the Massachusetts General Hosptial where he practiced psychiatry and studied neurology with Edward W. Taylor. He also worked with Walter Cannon in physiological research. Edsall was also instrumental in helping Cobb obtain financial support for two years in England, France, and Germany to study neuropathology and histology.

When Cobb returned to Boston Edsall was the full-time dean at Harvard Medical School and had plans for setting up a department of neurology with Cobb as its head. Cobb was to divide his time between teaching and research in neuropathology at the medical school and clinical work and teaching neurology at Boston City Hospital. In both places, in collaboration with William Lennox, his research was related to epilepsy. Lennox came to work with Cobb in 1921 and followed him to Boston City Hospital when the new neurological unit was opened in 1930 with Cobb as chief. Cobb remained at Boston City Hospital until 1934. It was during these four years that Jacob Finesinger came to work with him to study cerebral circulation and Frederick Gibbs to work in electroencephalography.

Cobb has a speech problem — he had stammered from early childhood. While in medical school and later in Baltimore he became interested in psychoanalysis in the hope that it would help his speech. Over the next few years he was analyzed three times with some improvement.

Cobb had been interested in the Boston Psychoanalytic Society for some time, and when the society was reorganized in 1930 he became quite active in it. During the mid-1930s Cobb belonged to a group in Boston who were instrumental in bringing outstanding psychiatrists and analysts to the city from Germany and Austria. Among them were Helene and Felix Deutsch and Hans Sachs, a lawyer and analyst. Cobb had a training



© 1987, Pfizer Inc.

VERYTHING

Effective control time and time again[1]

Effective control of fasting and postprandial glucose—patient after patient, meal after meal, year after year.

Insulin when it's needed

Insulin levels are rapidly elevated in response to a meal, then return promptly to basal levels after the meal challenge subsides.

Timed to minimize risks

Rapidly metabolized and excreted, with an excellent safety profile.[1] As with all sulfonylureas, hypoglycemia may occur.

In concert with diet in non-insulin-dependent diabetes mellitus

Glucotrol®

(glipizide) 5-mg and 10-mg Scored Tablets

SYNCHRONIZED SULFONYLUREA THERAPY

Please see brief summary of Glucotrol® (glipizide) prescribing information on next page.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Reference:
1. Sachs R, Frank M, Fishman SK. Overview of clinical experience with glipizide. In *Glipizide: A Worldwide Review*. Princeton, NJ: Excerpta Medica; 1984; pp 163-172.

GLUCOTROL® (glipizide) Tablets
Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19, supp. 2:747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur.

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hyperglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly fetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This fetotoxicity has been similarly noted with other sulfonylureas such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects: Prolonged severe hypoglycemia has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Chloestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia and pancytopenia have been reported with sulfonylureas.

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours since hypoglycemia may recur after apparent clinical recovery. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL (glipizide), dialysis is unlikely to be of benefit.

DOSAGE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL; in general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100. 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-65) Bottles of 100.

CAUTION: Federal law prohibits dispensing without prescription.

More detailed professional information available on request.

ROERIG Pfizer A division of Pfizer Pharmaceuticals
New York, New York 10017

© The Advertising Council, 1985

"YOU'D DIE IF YOU HAD MY JOB."

YOU COULD LEARN A LOT FROM A DUMMY. BUCKLE YOUR SAFETY BELT.

A Public Service Message Ad Council U.S. Department of Transportation

Motrin® 800 mg TABLETS
ibuprofen

Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886-1986

© 1986 The Upjohn Company

J-6138 January 1986

For moderate-to-severe vasomotor symptoms

PREMARIN®
(Conjugated Estrogens Tablets)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

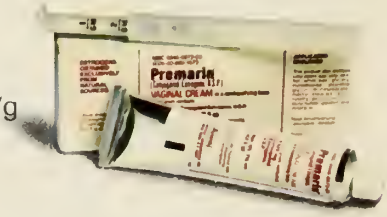
The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(Conjugated Estrogens)

Vaginal Cream

0.625mg/g



BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP): Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) **Osteoporosis (abnormally low bone mass).** Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy. (See Boxed Warning.) 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nontatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration. As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis, change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine, dizziness, mental depression, chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema, changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically* Female castration. Osteoporosis. Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control. Osteoporosis —0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off).

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three-to-six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Whitehead MI, Townsend PT, Pryse-Davies J, et al: Effects of estrogens and progestins on the biochemistry and morphology of the postmenopausal endometrium. *N Engl J Med* 1981;305:1599-1605. **2.** Paterson MEL, Wade-Evans T, Sturdee DW, et al: Endometrial disease after treatment with oestrogens and progestogens in the climacteric. *Br Med J* 1980;280:822-824. **3.** Magos AL, Brincat M, Studd JWW, et al: Amenorrhea and endometrial atrophy with continuous oral estrogen and progestogen therapy in postmenopausal women. *Obstet Gynecol* 1985; 67: 496-499. **4.** Whitehead MI, Lane G, Siddle N, et al: Avoidance of endometrial hyperstimulation in estrogen-treated postmenopausal women. *Semin Reprod Endocrinol* 1983;1:1;41-52. **5.** Barnes RB, Roy S, Lobo RA: Comparison of lipid and androgen levels after conjugated estrogen or depo-medroxyprogesterone acetate treatment in postmenopausal women. *Obstet Gynecol* 1985;66:216-219.

© 1986 Ayerst Laboratories

Ayerst AYERST LABORATORIES
New York, NY 10017

T6194/886

ROCHE
ME
MEDICATION
EDUCATION

The *New* Roche Product Books

- **Offer a supplement to, not a substitute for, patient contact**
- **Support your specific instructions to the patient**
- **Provide a permanent general reinforcement of your oral counseling**

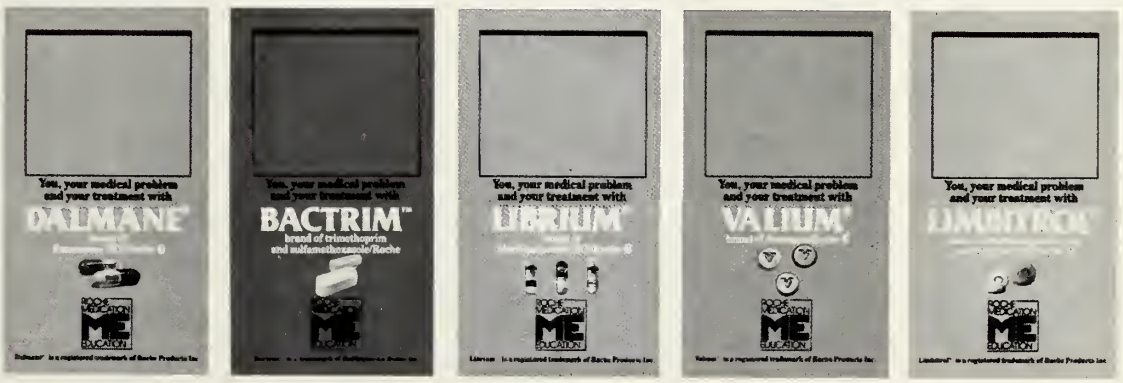
An ongoing Roche commitment to patient education

Roche has always believed that knowledge is each individual's key to good health and has long been committed to providing health care information to both professionals and the public. However, we have also always believed that the health care professional is and should be the prime source of medication information to patients. The Roche Medication Education (ME) program, begun in 1978, is one example of this commitment.

In the past seven years, over 50 million "WHAT IF" and "HOW TO" booklets have been provided by Roche for distribution to patients by physicians and other health care professionals.

Because you are the prime source of medication information for your patients, we invite you to look over the booklets listed below and request a complimentary supply of those applicable to your practice.

Complete the coupon and mail it to Professional Services Department, Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, New Jersey 07110.



☐ ☐ ☐ ☐ ☐

NAME

STREET ADDRESS

CITY STATE ZIP

ROCHE®
Medicines that matter
from people who care

ROCHE MEDICATION ME EDUCATION

We Wrote the Books on Patient Medication Education...

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

You, your medical problem and your treatment with

DALMANE®

brand of flurazepam HCl/Roche ©

You, your medical problem and your treatment with

LIBRIUM®

brand of chlordiazepoxide HCl/Roche ©

You, your medical problem and your treatment with

BACTRIM™

brand of trimethoprim and sulfamethoxazole/Roche

You, your medical problem and your treatment with

VALIUM®

brand of diazepam/Roche ©

You, your medical problem and your treatment with

LIMBITROL®

brand of chlordiazepoxide and amitriptyline HCl/Roche ©

ROCHE®

Copyright ©
1986 by Hoffmann-La Roche Inc.
and Roche Products Inc.
All rights reserved.

To order a complimentary supply of Roche Product Books, please see preceding page.

Rhode Island Medical Journal

May 1987
Volume 70, Number 5

Some perspectives in developing appropriate long-term care services
See page 213

CONTRIBUTIONS

205 Holistic Health: Implications for Physicians In a Changing World

213 Some Thoughts on Long Term Care

217 Physician Screening Practices and Colorectal Cancer Screening Prevalence Among the Rhode Island Population

203 EDITORIAL

204 INFORMATION FOR AUTHORS

Rhode Island

ADVERSE DRUG REACTION
Reporting Project

SUSPECT A SERIOUS OR UNEXPECTED

ADVERSE DRUG REACTION?

Please Report It.

SUSPECTED ADVERSE REACTION REPORT (For All Drugs and Biologics)

IMPORTANT: SUBMISSION OF A REPORT DOES NOT NECESSARILY CONSTITUTE AN ADMISSION THAT THE DRUG CAUSED THE ADVERSE REACTION

PATIENT INITIALS (Optional)	AGE (Years)	SEX	DATE OF REACTION ONSET
A.D.R.	54	☑ MALE ☐ FEMALE	12 Oct. 1986

DESCRIBE REACTION(S) (Give signs, symptoms, diagnoses, course and lab findings)

JAUNDICE

CHECK ALL APPROPRIATE TO REACTION
- ☐ DIED
- ☑ TREATED WITH Rx DRUG
- ☑ INPATIENT HOSPITALIZATION
- ☐ SEVERE OR PERMANENT DISABILITY
- ☐ EMERGENCY ROOM TREATMENT
- ☐ TREATMENT IN PHYSICIAN OFFICE
- ☐ NONE OF THE ABOVE

SUSPECTED DRUG(S) (Trade Name is preferred. If a generic product, give manufacturer. Indicate Lot No. for vaccines, biologics)

[redacted]

REASON FOR USE OF DRUG(S)	ROUTE	TOTAL DAILY DOSE	DATES OF ADMINISTRATION
HYPERTENSION	P.O.	100mg.	9 Sept.- 12 Oct. '86

OTHER DRUGS TAKEN CONCOMITANTLY (Exclude those used to treat reaction)

None

OTHER RELEVANT HISTORY (e.g., Concomitant Diagnoses, Pregnancy, etc.)

None

PHYSICIAN NAME AND TELEPHONE NUMBER

J. Doe, M.D. 277-2550

Confidential

ALSO REPORTED TO MANUFACTURER ☑ YES ☐ NO

For report forms, guidelines and information contact S. Rosenbaum, PhD, 277-2901

A pilot project of the Rhode Island Department of Health
sponsored by the U.S. Food and Drug Administration

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were treated merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

NOW AVAILABLE...
NEW LOW DOSE
INDERAL® LA 60 mg
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. INDERAL LA is formulated to provide a sustained release of propranolol hydrochloride. INDERAL LA is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor-blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (60, 80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL Tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours, then decline exponentially.

INDERAL LA should not be considered a simple mg-for-mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension. It may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

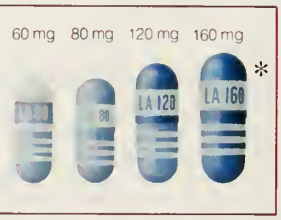
CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first-degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES



WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely; or INDERAL should be discontinued (gradually if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (eg, chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta blockers should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. Following insulin-induced hypoglycemia, propranolol may cause a delay in the recovery of blood glucose to normal levels.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol may change thyroid function tests, increasing T_4 and reverse T_3, and decreasing T_3.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. GENERAL. Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

CLINICAL LABORATORY TESTS. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Caution should be exercised when patients receiving a beta blocker are administered a calcium-channel-blocking drug, especially intravenous verapamil, for both agents may depress myocardial contractility or atrioventricular conduction. On rare occasions, the concomitant intravenous use of a beta blocker and verapamil has resulted in serious adverse reactions, especially in patients with severe cardiomyopathy, congestive heart failure or recent myocardial infarction.

Aluminum hydroxide gel greatly reduces intestinal absorption of propranolol.

Ethanol slows the rate of absorption of propranolol.

Phenytoin, phenobarbitone, and *rifampin* accelerate propranolol clearance.

Chlorpromazine, when used concomitantly with propranolol, results in increased plasma levels of both drugs.

Antipyrine and *lidocaine* have reduced clearance when used concomitantly with propranolol.

Thyroxine may result in a lower than expected T_3 concentration when used concomitantly with propranolol.

Cimetidine decreases the hepatic metabolism of propranolol, delaying elimination and increasing blood levels.

Theophylline clearance is reduced when used concomitantly with propranolol.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

PREGNANCY. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose. There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS. INDERAL is excreted in human milk. Caution should be exercised when INDERAL (propranolol HCl) is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. Bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. Light-headedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, vivid dreams, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics. For immediate formulations, fatigue, lethargy and vivid dreams appear dose related.

Gastrointestinal. Nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. Pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. Bronchospasm.

Hematologic. Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. Alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL Tablets to INDERAL LA Capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg-for-mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three- to seven-day intervals until optimal response is obtained. Although individual patients may respond at any dosage level, the average optimal dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimal migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximal dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

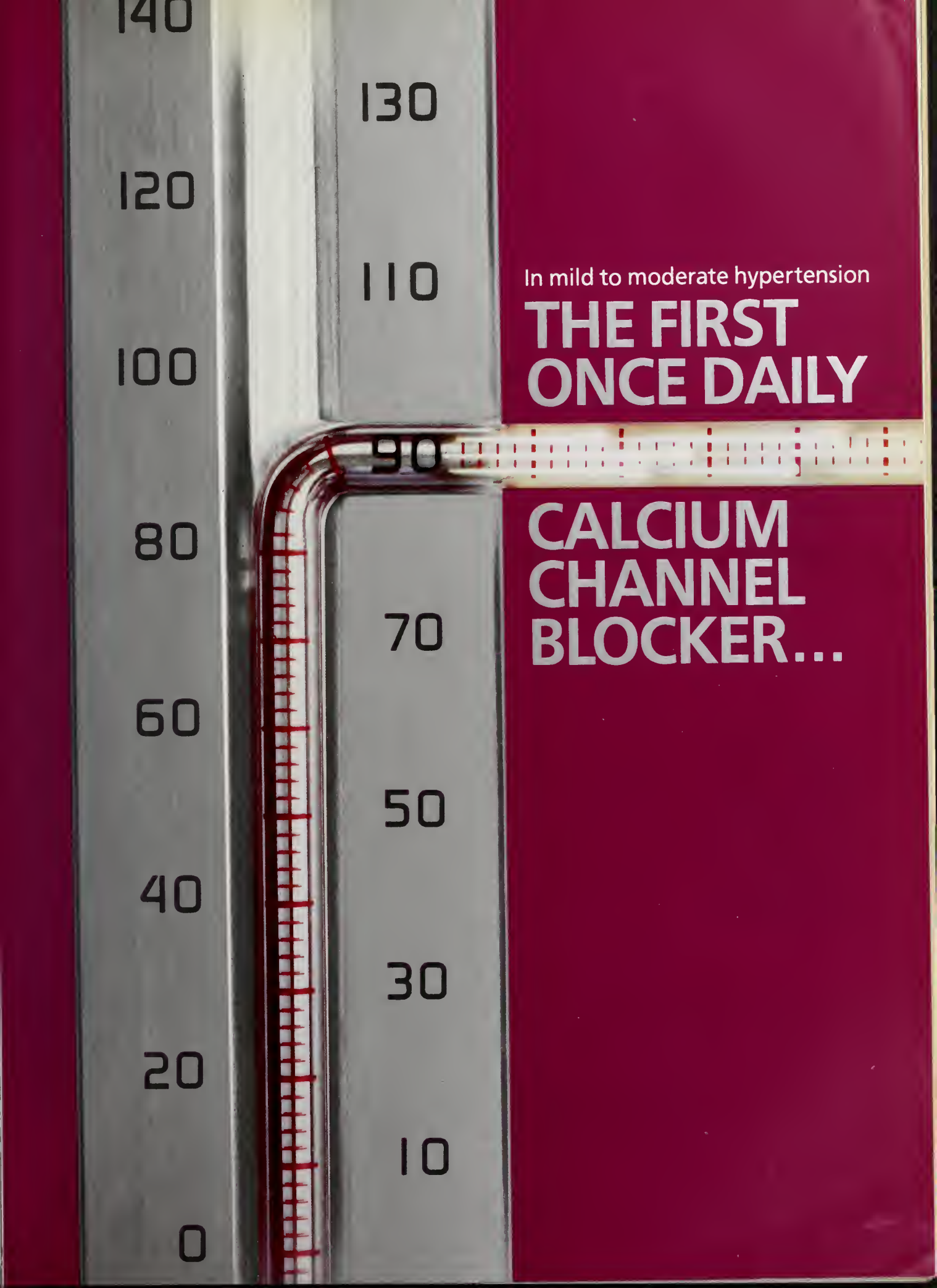
REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985; 145: 1321-1323.

R 7119/587

Ayerst AYERST LABORATORIES
New York, NY 10017

© 1987 Ayerst Laboratories


140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
In mild to moderate hypertension
THE FIRST ONCE DAILY
CALCIUM CHANNEL BLOCKER...

NEW
ONCE DAILY

ISOPTIN SR*

(verapamil HCl/Knoll)

240 mg scored, sustained-release tablets

JAMES B.
38, black male, heavy smoker. Prescribed a diuretic by another physician last year for hypertension.

YOUR CONCERNS
Presents with "smoker's cough." Workup reveals a BP of 150/107.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Black hypertensives often have low plasma renin activity and generally do not respond favorably to beta blockers.
— Beta blockers may increase the likelihood of bronchospasm.

ALICE W.
65, diabetic, overweight. Her BP has elevated to 190/98.

YOUR CONCERNS
She's on daily insulin.

A LOGICAL CHOICE FOR CONTROL OF HER BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike most beta blockers and diuretics, ISOPTIN has no adverse effects on serum glucose levels.
— Unlike most beta blockers, ISOPTIN does not mask the symptoms of hypoglycemia.

THOMAS G.
70, asthmatic. In the past, BP adequately controlled with 25 mg hydrochlorothiazide daily.

YOUR CONCERNS
Today patient presents with symptoms of gout. Workup reveals high uric acid level, low serum potassium, and BP elevated to 180/98.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN will not decrease serum potassium levels or elevate uric acid levels.
— Unlike beta blockers, ISOPTIN can be used safely in asthma and COPD patients.

JOHN K.
42, Annual physical uncovered diastolic BP of 102... confirmed on three successive office visits. Unresponsive to nonpharmacologic intervention.

YOUR CONCERNS
Salesman, spends many hours of his working day in car... total cholesterol level 300, HDL 35.

A LOGICAL CHOICE FOR CONTROL OF HIS BP
ISOPTIN* (verapamil HCl/Knoll) because...
— Unlike diuretics, ISOPTIN does not cause urinary urgency.
— Unlike either beta blockers or diuretics, ISOPTIN will not adversely affect his already seriously compromised lipid profile.
— Unlike with propranolol, fatigue and impotence are rarely reported.

Antihypertensive therapy you and your patients can live with

*A product of Knoll research.

© 1986, BASF K & F Corporation

2538/2-87

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

BASF Group

knoll®

Printed in U.S.A.

Please see adjacent page for brief summary.

In mild to moderate hypertension

Brief Summary

THE FIRST ONCE DAILY CALCIUM CHANNEL BLOCKER

ISOPTIN® SR
(verapamil HCl/Knoll)
240 mg scored, sustained-release tablets

CONTRAINDICATIONS: 1) Severe left ventricular dysfunction (see WARNINGS), 2) Hypotension (less than 90 mmHg systolic pressure) or cardiogenic shock, 3) Sick sinus syndrome or 2nd or 3rd degree AV block (except in patients with a functioning artificial ventricular pacemaker).

WARNINGS: Heart Failure: ISOPTIN should be avoided in patients with severe left ventricular dysfunction (see DRUG INTERACTIDNS). Patients with milder ventricular dysfunction should, if possible, be controlled before verapamil treatment. Hypotension: ISOPTIN (verapamil HCl) may produce occasional symptomatic hypotension. Elevated Liver Enzymes: Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. Accessory Bypass Tract (Wolff-Parkinson-White): Patients with paroxysmal and/or chronic atrial flutter or atrial fibrillation and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous verapamil. While this has not been reported with oral verapamil, it should be considered a potential risk. Treatment is usually D.C.-cardioversion. Atrioventricular Block: The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1st degree AV block and transient bradycardia. Higher degrees of AV block, while infrequent (0.8%), may require a reduction in dosage or, in rare instances, discontinuation of verapamil HCl. Patients with Hypertrophic Cardiomyopathy (IHSS): Although verapamil has been used in the therapy of patients with IHSS, severe cardiovascular decompensation and death have been noted in this patient population.

PRECAUTIONS: Impaired Hepatic or Renal Function: Verapamil is highly metabolized by the liver with about 70% of an administered dose excreted in the urine. In patients with impaired hepatic or renal function verapamil should be administered cautiously and the patients monitored for abnormal prolongation of the PR interval or other signs of excessive pharmacological effects (see OVERDDSAGE).

Drug Interactions: Beta Blockers: Concomitant use of ISDPTIN and oral beta-adrenergic blocking agents may be beneficial in certain patients with chronic stable angina or hypertension, but available information is not sufficient to predict with confidence the effects of concurrent treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities. Digitalis: Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment increases serum digoxin levels by 50 to 75% during the first week of therapy and this can result in digitalis toxicity. Upon discontinuation of ISDPTIN (verapamil HCl), the patient should be reassessed to avoid underdigitalization. Antihypertensive Agents: Verapamil administered concomitantly with oral antihypertensive agents (e.g., vasodilators, angiotensin-converting enzyme inhibitors, diuretics, beta blockers, prazosin) will usually have an additive effect on lowering blood pressure. Patients receiving these combinations should be appropriately monitored. Disopyramide: Disopyramide should not be administered within 48 hours before or 24 hours after verapamil administration. Quinidine: In patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. There has been a report of increased quinidine levels during verapamil therapy. Nitrates: The pharmacologic profile of verapamil and nitrates as well as clinical experience suggest beneficial interactions. Cimetidine: Two clinical trials have shown a lack of significant verapamil interaction with cimetidine. A third study showed cimetidine reduced verapamil clearance and increased elimination to 1/2. Anesthetic Agents: Verapamil may potentiate the activity of neuromuscular blocking agents and inhalation anesthetics. Carbamazepine: Verapamil may increase carbamazepine concentrations during combined therapy. Rifampin: Therapy with rifampin may markedly reduce oral verapamil bioavailability. Lithium: Verapamil may lower lithium levels in patient on chronic oral lithium therapy. Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no evidence of a carcinogenic potential of verapamil administered to rats for two years. Verapamil was not mutagenic in the Ames test. Studies in female rats did not show impaired fertility. Effects on male fertility have not been determined. Pregnancy (Category C): There are no adequate and well-controlled studies in pregnant women. ISDPTIN crosses the placental barrier and can be detected in umbilical vein blood at delivery. This drug should be used during pregnancy, labor, and delivery, only if clearly needed. Nursing Mothers: ISOPTIN is excreted in human milk, therefore, nursing should be discontinued while verapamil is administered. Pediatric Use: Safety and efficacy of ISOPTIN in children below the age of 18 years have not been established.

ADVERSE REACTIONS: Constipation 8.4%, dizziness 3.5%, nausea 2.7%, hypotension 2.5%, edema 2.1%, headache 1.9%, CHF/pulmonary edema 1.8%, fatigue 1.7%, bradycardia 1.4%, 3° AV block 0.8%, flushing 0.1%, elevated liver enzymes (see WARNINGS). The following reactions, reported in less than 1.0% of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain; they are mentioned to alert the physician to a possible relationship: angina pectoris, arthralgia and rash, AV block, blurred vision, cerebrovascular accident, chest pain, claudication, confusion, diarrhea, dry mouth, dyspnea, ecchymosis or bruising, equilibrium disorders, exanthema, gastrointestinal distress, gingival hyperplasia, gynecomastia, hair loss, hyperkeratosis, impotence, increased urination, insomnia, macules, muscle cramps, myocardial infarction, palpitations, paresthesia, psychotic symptoms, purpura (vasculitis), shakiness, somnolence, spotty menstruation, sweating, syncope, urticaria. Treatment of Acute Cardiovascular Adverse Reactions: Whenever severe hypotension or complete AV block occur following oral administration of verapamil, the appropriate emergency measures should be applied immediately, e.g., intravenously administered isoproterenol HCl, levarterenol bitartrate, atropine (all in the usual doses), or calcium gluconate (10% solution). If further support is necessary, inotropic agents (dopamine or dobutamine) may be administered. Actual treatment and dosage should depend on the severity and the clinical situation and the judgment and experience of the treating physician.

OVERDOSAGE: Treatment of overdosage should be supportive. Beta-adrenergic stimulation or parenteral administration of calcium solutions may increase calcium ion flux across the slow channel, and have been used effectively in treatment of deliberate overdosage with verapamil. Clinically significant hypotensive reactions or fixed high degree AV block should be treated with vasopressor agents or cardiac pacing, respectively. Asystole should be handled by the usual measures including cardiopulmonary resuscitation.

Knoll Pharmaceuticals
A Unit of BASF K&F Corporation
Whippany, New Jersey 07981

knoll®

BASF Group

©1986, BASF K&F Corporation 2474/11/86 Printed in U.S.A.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

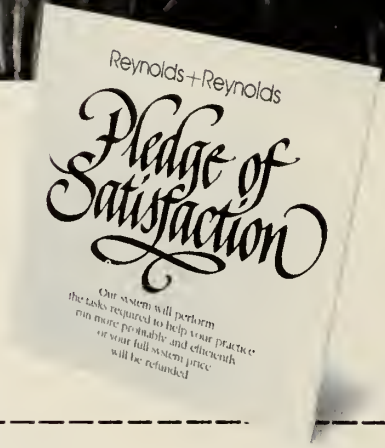
GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

Are You Concerned About the Competence of a Certain Physician?

If so, the Peer Review Committee on Physician Competency can offer discreet and effective help. A standing committee of the Rhode Island Medical Society since 1985, the Peer Review Committee works in a completely confidential, supportive way to help assure that physicians consistently meet minimum acceptable standards of medical practice. The primary work of the Committee is to help physicians improve the quality of their care through education.

If you know a physician who can benefit from peer education in a particular area of medical practice, please write Dr. William Colaiace, Chairman, Peer Review Committee on Physician Competency, Rhode Island Medical Society, 106 Francis Street, Providence, RI 02906. For more information, call the Society at (401)331-3207. All referrals are held in strict confidence.

YOU DON'T OFFER A WRITTEN GUARANTEE UNLESS YOU HAVE THE BEST COMPUTER SYSTEM.



Introducing the Reynolds and Reynolds Pledge of Satisfaction.

Before we decided to offer your practice a written guarantee, we made sure we had the best medical practice management system on the market.

Only Reynolds + Reynolds, a Fortune 500 company with over 20 years of computer experience as a single source supplier, offers you:

- State-of-the-art hardware from IBM, NCR, and Texas Instruments.
- The most comprehensive Unix-based medical practice management software in the industry.
- MPMS-PLUS software features:
  - appointment scheduling
  - patient billing
  - accounts receivable
  - insurance claims
  - management reports.
- The industry's most responsive after-sale hardware and software service and support.
- Competitive lease plan rates.
- A full line of computer forms.
- A unique written pledge of satisfaction assuring you that our system will perform the tasks required to help your practice run more profitably and efficiently or your full system price will be refunded.

Whether you're a new buyer or a dissatisfied system user, Reynolds + Reynolds' single source concept is right for you. Interested? To know more about our MPMS-Plus System and our Pledge of Satisfaction, fill out the attached coupon or call us toll-free at 1-800-632-4278 (in Ohio call 1-800-535-7128.)

Reynolds+Reynolds®
P.O. Box 1005
Dayton, OH 45401

Committed To Your Future

Yes, I'm interested! I want to know more about the Reynolds + Reynolds® MPMS-PLUS system. To make our first discussion more efficient, I've filled in the information requested below.

I'm considering automating my practice:

☐ Right away. ☐ In six months. ☐ In a year or so.

☐ I'd like to know more about your unique Pledge of Satisfaction.

Name: _____

Practice Name: _____

Address: _____

City: _____ State: _____ Zip: _____

Phone: _____

# of Physicians: ____ Specialty: _____

May 1987
Volume 70, Number 5

Rhode Island Medical Journal

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA
MAY 21 1987

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Guy A. Settipane, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

***Edward R. Feller, MD**

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Peter D. T. Clarisse, MD
President

Richard G. Bertini, MD
President-Elect

Milton W. Hamolsky, MD
Secretary

Kenneth E. Liffmann, MD
Treasurer

Herbert Rakatansky, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

We've Reduced the Rates on Our 5 Year Renewable Group Term Life Insurance

Take Advantage of Your Group Purchasing Power

$100,000.00

Non-Smoker Rates

ANNUAL COST

AGE	MALE		FEMALE	
	OLD	NEW (NON SMOKER PREMIUM)	OLD	NEW (NON SMOKER PREMIUM)
Under 30	$ 107.00	$ 79.00	$ 86.00	$ 63.00
30–34	$ 119.00	$ 81.00	$ 94.00	$ 65.00
35–39	$ 169.00	$116.00	$116.00	$ 87.00
40–44	$ 299.00	$185.00	$202.00	$147.00
45–49	$ 515.00	$319.00	$346.00	$241.00
50–54	$ 861.00	$510.00	$576.00	$380.00
55–59	$1,293.00	$859.00	$864.00	$627.00

1) Maximum Benefit available for member $300,000.00
2) Full Benefit to Age 70
3) Conversion Benefit Without Medical Evidence to a Permanent Life Plan
4) Waiver of Premium Benefit Included
5) No Physical Examination Required
6) Coverage for Spouse up to $150,000

Endorsed by the
RHODE ISLAND MEDICAL SOCIETY

The Administrators
LB personal service since 1922
LESTER L. BURDICK, INC.
Loyalty Group Insurance
10 POST OFFICE SQUARE, BOSTON, MA 02109
(617) 426-0020

Underwritten by: **COMMERCIAL INSURANCE COMPANY** 15 Corporate Place South, Piscataway, NJ 08854. 201/981-4842

Rhode Island Medical Journal Volume 70, Number 5 May 1987

TABLE OF CONTENTS

203 **EDITORIAL**

The Paradox of DRGs

Seebert J. Goldowsky, MD

CONTRIBUTIONS

205 **Holistic Health: Implications for Physicians In a Changing World**

A Basic Element is the Encouragement, When Appropriate, of Patient's Independence and Responsibility

John M. Wiecha

213 **Some Thoughts on Long Term Care**

H. Denman Scott, MD, MPH

217 **Physician Screening Practices and Colorectal Cancer**

Screening Prevalance Among the Rhode Island Population Experience is Comparable to that Reported Nationally

Susan Masterson-Allen, MA
Vincent Mor, PhD
M. Peter Lance, MD

COVER: *Photograph courtesy of the Jewish Home, 99 Hillside Avenue, Providence, RI.*

The Trustees of the Fiske Fund of the Rhode Island Medical Society are pleased to announce the

FISKE PRIZE FOR 1987

to be awarded for an original contribution on

"AIDS Pandemic . . . Etiology, Incidence, Distribution, & Control"

The award is named after Caleb Fiske (1753-1834), who was a Rhode Island physician and judge, Army surgeon, and a descendent of Roger Williams. Since the prize was initiated in 1836, 87 awards have been made for original contributions. Previous recipients include Charles V. Chapin, Providence, internationally known for his research on public health; David King, Jr., Newport who received the award in 1836 for his paper on "Purpura Haemorrhagica: Its Causes and Treatment"; and Alton Oschner, New Orleans, who received the 1958 award for his paper entitled "Bronchyogenic Carcinoma: Predisposing Causes."

The award for the 1987 Fiske Prize will be a maximum of $2,500. The Trustees reserve the right to award one or more prizes. The competition is not restricted to physicians.

Guidelines:

1) The original and one copy must be submitted by Aug. 24, 1987 to Secretary, Caleb Fiske Fund of the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903.
2) All papers must be double-spaced and should not exceed 10,000 words.
3) The award recipient must transfer copyright privileges to the Trustees of the Caleb Fiske Fund of the Rhode Island Medical Society. The paper will be considered for publication in the *Rhode Island Medical Journal*, subject to review by the Editorial Board.
4) The award recipient will also present his/her prize winning paper at a symposium to be scheduled in the Fall commemorating the 175th anniversary of the Rhode Island Medical Society.

EDITORIAL

The Paradox of DRGs

The advent of prospective payment of Medicare Part A hospital bills by Diagnostic Related Groups (DRGs) had most hospital administrators in panic as implementation approached. Recent information, however, indicates that their fears were greatly exaggerated. Hospital "profits" have unexpectedly risen, rather than fallen, under the DRG system. According to the Congressional Budget Office (CBO), profits were at least 15.7 per cent in 1986 and at least 17.6 per cent in 1985. Furthermore, the budget office, the inspector general of the Department of Health and Human Services (DHHS), and an advisory commission established by Congress have found that hospital profits related to Medicare in 1984, the first year of DRGs, was 12 to 15 per cent. With this effect demonstrated three years in a row, it appears to be more than an accident.

These financial gains were realized even though the number of Medicare patients admitted to the hospitals declined steadily from 11.8 million in 1983 to 10.8 million in 1986. The profits appear to have resulted from several factors; the success demonstrated by hospitals in controlling costs; a dramatic reduction in the length of hospital stays, perhaps in some cases reflecting premature discharge of patients; and projections used in setting the Medicare payment scale. There is no indication that pervasive improper actions by hospitals were a factor.

These results understandably have provoked lively debate in Congress, where there will surely be a move to cut Medicare payments. Hospital administrators predictably complain that such cuts would affect adversely the quality of care and access to care for millions of prospective patients. If Medicare payments are cut, they maintain, charges for patients covered by other plans will inevitably increase.

Under the DRG system a hospital can retain the surplus payment if the costs of treating a patient are less than the reimbursement from government. The American Hospital Association maintains that hospitals must earn a surplus if they are to be protected against unpredictable fluctuations in revenue from other sources. Further, it argues that Congress provided an opportunity for hospitals to earn a surplus in the hope that they would become more efficient and productive. It would be patently unfair, they say, to penalize them for responding to those incentives.

Richard P. Kusserow, inspector general of DHHS, has for some time been claiming that hospitals were making undeserved profits; but some Congressmen have considered these assertions to be politically motivated to justify cutbacks by the Reagan administration. But similar estimates by the CBO and the Prospective Payment Assessment Commission (PPAC), a federal advisory panel, have brought the matter to the fore.

Professor Stuart H. Altman of Brandeis University, chairman of the PPAC, has concluded that in 1984 and 1985 "there is no question that the hospital industry as a whole received Medicare payments greater than anticipated, indeed substantially in excess of what even the hospitals anticipated."

A recent study of 236 hospitals, according to Kusserow, revealed that a 1,000 bed facility in Ohio had netted $30 million on $99 million dollar payments, a profit of 31 per cent. A Missouri hospital of 650 beds made a profit of $25 million on revenues of $58 million, or 43 per cent. The Medicare profits for 1984 as quoted above were based on an analysis of all Medicare reports, while those for subsequent years were based on samples.

Rhode Island hospitals have been strangely silent amidst these developments, suggesting that that they too have done pretty well. It will be interesting to see how this drama plays out. Is anyone willing to bet that DRG payments will not be reduced?

Seebert J. Goldowsky, MD

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

Holistic Health: Implications for Physicians in a Changing World

A Basic Element is the Encouragement, When Appropriate, of Patient's Independence and Responsibility

John M. Wiecha

Why should we be interested in holistic health, and just what is it anyway? As will become apparent, the definition is a subjective one. A major purpose of this paper is to provide health professionals with some concepts with which to understand the variety of disciplines operating under this rubric. In addition, with increasing numbers of people seeking these health alternatives, it is vital for more conventional practitioners to understand the reasons for their growing popularity (such as dissatisfaction with the conventional).

The controversy over the authenticity of holistic health practices sits squarely in the middle of a fascinating debate over the appropriate nature of health care itself. Also considerable controversy surrounds the correct definition of holistic health. Most authors writing on the subject would agree on the following general one: "holistic medicine takes a broad view of human functioning. It views the human being as an open system that seeks to preserve internal harmony between the total organism and the biological and social environment. Disease is considered a perturbation of the whole system and health as harmony. Treatment is, therefore, aimed at putting the system back into smooth functioning through working at spiritual, psychological and social, as well as bodily levels."[1]

Why is the public becoming increasingly interested in holistic health and what does this imply? A variety of explanations exist: some argue that it represents a cyclical public dissatisfaction with conventional medicine,[2] while others dismiss this as nonsense. Most would agree, however, that holistic health's growing popularity reflects perceived limitations of conventional medicine and a dissatisfaction with current health care practices and institutions. It is no secret that public opinion of the medical profession is low and declining. Two-thirds of the American public now believe that people are beginning to lose faith in doctors, and the same fraction believe doctors are too interested in making money.[3]

John M. Wiecha is currently a fourth-year medical student at SUNY Stony Brook School of Medicine. He graduated from Brown University in 1981 and recently worked with Dr. Lois Monteiro in Brown University's Community Medicine Department, and with the Pawtucket Heart Health Program.

Less than half of persons surveyed recently felt that doctors explain things well, and this represents a full ten per cent fall in two years.[4] Clearly, people are not content with conventional medicine. This stems not merely from resentment over high physician income, but rather from more fundamental sources. Physicians' preoccupation with making money might not be objectionable to the public if they felt that they were receiving the kind of care that they need and expect, if doctors were explaining things to them, and if they did not feel powerless and incapable of participating in their own care.

Clearly people's dissatisfaction is not with their doctors technical competence. Over seventy per cent of the public believes that physicians are up on the latest advances in medicine, and about ninety per cent agree that their doctor is available for routine health problems.[4] The loss of faith in the profession, and the public's search for alternatives, therefore, has other identifiable and related causes: 1) loss of faith in medical technology, 2) rejection of a technological approach to health care, and 3) lack of autonomy in the conventional patient role. I will discuss each of these separately.

The loss of faith in medical technology. This is a popular topic. We are frequently reminded that the really significant advances in disease control and the increasing life span result not from curative medicine, but from public health preventive measures begun at the turn of the century. This is controversial. To quote one author: "By providing more accurate diagnosis, identifying the sources of infection and their modes of transmission, and diffusing knowledge of personal hygiene, medicine entered directly into the improved effectiveness of public health."[5] Yet, undeniably, the medical field can in some instances be accused of hyperbole. The success of the so-called "war on cancer" is a good example of failed expectations. In this most terrifying of diseases, medical doctors have repeatedly claimed significant progress in overall prognosis. However, reports frequently come out challenging these assertions. One recent major review claims that increasing survival rates for cancer victims actually reflect earlier diagnosis, not more effective treatment.[6] Medicine has perhaps set itself up for failure by creating unreasonably high expectations in patients resulting in inevitable dissatisfaction. The current epidemic of malpractice litigation is perhaps another reflection of this phenomenon.

Rejection of a technological approach to health care. To oversimplify, biomedical medicine is based on the world view of scientific materialism. In this paradigm the world of objects is seen as a self-contained system and things are related to each other solely by the laws of cause and effect. Psychological and spiritual phenomena are irrelevant to the causal chain. Our bodies are composed of matter, and health and disease can be defined in material terms. Health, in this allopathic system, is defined negatively as the absence of disease. As one author puts it: "The doctor is an applied scientist who seeks to bring the most up to date scientific knowledge to bear on diagnosis and treatment. The patient's body is the arena in which the battle between the physician and the pathogenic process is fought."[1] This type of medicine is based on the presumption that scientific inquiry is the only valid way to discover truth, and phenomena that are purely subjective are ignored or dismissed. Miles points out that in the past, this reductionist view of the life process was humanized by the relationships between physician and patients. However, "as medicine became more scientific and technological, and less based on the physician/client relationship, the impact of this perspective has become more apparent."[7] This system has proved to be effective in treating infectious processes and structural problems, but marginally so in dealing with chronic degenerative disease and lifestyle problems (eg, drug abuse, stress).

The approach of the modern physician emphasizes the manipulation of nature, and critics of this philosophy argue that one result may be overzealous and intrusive medical therapy. Iatrogenesis is a classic example, and indications are that this problem is epidemic. Five per cent of all hospital admissions are reportedly precipitated by complications of diagnostic and therapeutic procedures, and nearly twenty per cent of all hospitalized patients may expect to have at least one condition caused by medical management, for which the fatality may run as high as thirteen per cent.[8]

That doctors are not compassionate is another commonly heard criticism along these same lines. In a recent television documentary, a father recounted the experience of being told of his son's imminent death. The oncologist coldly and briefly told the father only the number of months of life remaining, and then quickly turned and walked away. Some have attributed such attitudes to inadequate teaching, pointing out that a medical student is apt to encounter far greater criticism for ignorance of a medical fact than for

incompetence in dealing with people as human beings. Whatever the cause, it is clear that some important aspects of doctor-patient relationships seem to have been obscured, even as technological-medical competence is improving. Patients are saying that the former is at least as important as the latter.

Lack of autonomy in the conventional patient role. This is actually one of the major arguments used by holistic healers to demonstrate that in some respects allopathic medicine is antithetical to health. A similar position is articulated by some philosophers, probably originally and most forcibly by Ivan Illich, who opens *Medical Nemesis* with the assertion that "the medical establishment has become a major threat to health." He writes:

". . . the so-called health professions have . . . a culturally health denying effect insofar as they destroy the potential of people to deal with their human weakness, vulnerability, and uniqueness in a personal and autonomous way. The patient in the grip of contemporary medicine is but one instance of mankind in the grip of its pernicious techniques. This cultural iatrogenesis . . . is the ultimate backlash of hygienic progress and consists in the paralysis of healthy responses to suffering, impairment, and death. It occurs when people accept health management designed to the engineering model. . . ."[9]

Physicians, it is argued, have used the weapon of their scientific knowledge effectively to subjugate the patient into a role of a submissive and deferential obeyer of instructions. The person responsible for successful outcome of treatment is not the patient, but primarily the provider.

Another commonly used metaphor is a religious one. The doctor in some regard commands religious respect and authority. Medicine has, according to one defender of this interesting idea, "promoted a set of beliefs, symbols, and institutions that have direct analogy to ecclesial structures and the ideology of medicine implies that life itself is a disease to be cured or, at best, prevented."[10] In one recent book, a doctor writes about the issue of whether or not it is appropriate to "play God."[11]

The idea that each individual should be responsible for his or her own health is obvious. Yet many medical authorities write of this as a new concept, perhaps not realizing that the nature of the encounter between doctor and patient has frequently been a relationship of informed-uninformed, or enlightened-ignorant. People have been taught not to trust in their own assessment of health and to believe that they are incapable of understanding their own bodies.

Summary

I have discussed in general some aspects of the public's increasing dissatisfaction with conventional medicine. A technological aloofness often exists. For some people questions exist about the desirability of treatment and patients often feel ignorant or stupid. These factors, as well as the occasional outright failure of conventional medicine, create great interest in alternative styles of healing. Some are useful, some dangerous, but the phenomenon of their growing popularity serves as a critical lesson for more conventional healers. This lesson will doubtless continue to be ignored by many medical doctors. In 1981 at the annual meeting of the Association of American Physicians, Doctor Donald Seldin in his presidential address, presented a definition of medicine which excluded all concepts except those of biomedical science. He stated ". . . medicine is a very narrow discipline. Its goals may be defined as the relief of pain, the prevention of disability, and the postponement of death by the application of the theoretical knowledge incorporated in medical science to individual patients."[12] Perhaps only after scientific validation of holistic concepts, such as the importance of patient responsibility and cooperation in health care, will these issues find greater acceptance. For such people I refer to a recent report demonstrating that measures of ego strength, life stress, socioeconomic status, and family functioning are independent predictors of physical health.[13]

It is not our intention in this paper to provide a survey of all the various techniques used by holistic health practitioners. There are many, and the scope of the movement appears virtually unlimited. What has been stressed, however, is the desirability of accepting and practicing a basic element of holism — that of encouraging, when appropriate, a patient's independence and responsibility. In this context the physician is a guide, a facilitator, and, most importantly, an educator. Many reports encourage physicians to pay particular attention to their communication skills, as this correlates with patient satisfaction and compliance.[14] For an excellent overview of holistic health, the reader may wish to refer to *The Holistic Health Handbook,* written by the Berkeley Holistic Health Center.[7]

References

1. Frank, JD: Holistic Medicine — A view from the Fence. The Johns Hopkins Med J 1981;149:222-227.
2. Geyman, JP: Holistic Health Care: Neither New Nor Coherent. The J Fam Pract 1984;19:727-728.
3. Mechanic, D: Public Perceptions of Medicine: New Engl J Med 1985;312:1181-1183.
4. Lundberg, GD: Editorial: Medicine — A Profession in Trouble? JAMA 1985;253:2879-2880.
5. Starr, P: Social Transformation of American Medicine. New York, Basic Books, Inc, 1982.
6. Cairns, J: The Treatment of Diseases and the War Against Cancer: Sci Am, Nov. 1985;253, No. 5:51-59.
7. The Holistic Health Handbook, Bauman. Brint, Piper, and Wright, Published by And/Or, Berkeley, CA, 1978.
8. Freidman, M: Iatrogenic Disease Addressing a Growing Epidemic. Postgrad Med 1982;Vol. 71, No. 6:pp. 123-129.
9. Illich, I: Medical Nemesis. New York, Pantheon Books, 1976.
10. Raymond, J: Medicine as Patriarchal Religion. J Med Philos, May 1982;7(2):197-216.
11. Hilfiker, D: Healing the Wounds. New York, Pantheon, 1985.
12. Perkoff, G: The Boundaries of Medicine. J Chronic Dis 1985; 38:271-278.
13. Blotcky, A: Holistic Model of Health. Based on a poster session at the annual meeting of the American Psychosomatic Society, 1981.
14. Bartlett, E, et al: The Effects of Physician Communication Skills on Patient Satisfaction; Recall and Adherence. J Chron Dis 1984;37:755-764.

138 Linden Street
Wellesley, MA 02181

HOME NURSING CARE

Private Duty Nursing

* REGISTERED NURSES
* LICENSED PRACTICAL NURSES
* NURSE AIDES
* HOMEMAKERS
* HOME HEALTH AIDES

When Home Care Is Needed

Please Call . . .

CATHLEEN NAUGHTON ASSOCIATES

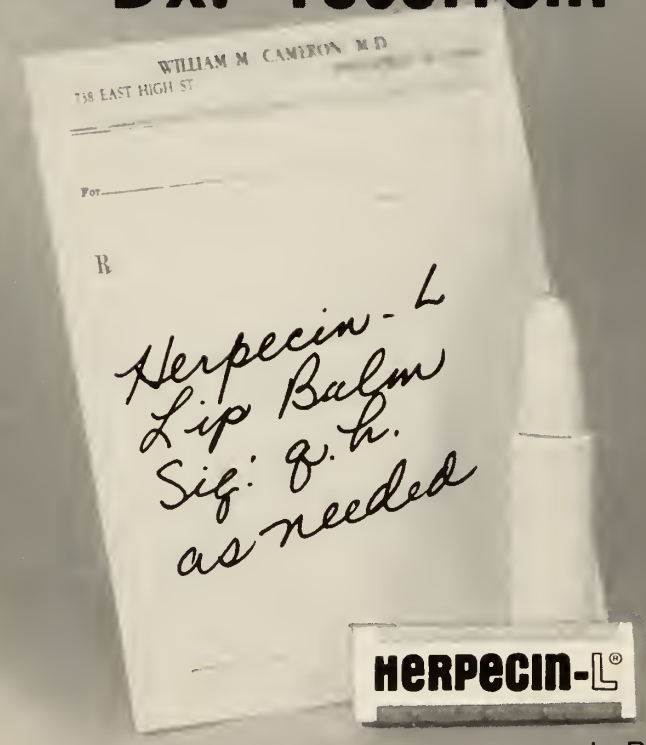
Employes Bonded and Insured

cna

(401) 751-9660

Available 7 days a week
24 hours a day.

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms . . .** blisters **never formed . . .** remarkable." DH, MA

"(In clinical trials) **. . . response** was **dramatic. HERPECIN-L . .** proven **far superior.**" DDS, PA

"All patients claimed **shorter duration . . .** at **prodromal symptoms . . .** HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

FOR RENT
WESTERLY AREA

Two Doctor's Offices
Fully Equipped

Write to:

Dr. Louis Morrone
8 Oaklawn Terrace
Westerly, RI 02891

THE YACHT HEADQUARTERS
AT BEND BOAT BASIN

Your Season to Sail. . .

begins right here. We'll show you something that'll make this summer one long pleasure cruise — no matter what your budget, no matter how extensive or limited your experience.

Choose from the all-new **Freedom** line, the renown quality of **Sabre** or the diversity of **Pearson** Yachts. For the performance-oriented, see the **Tripp 37**.

Hungry for Power?

At Yacht Headquarters, there's a powerboat to suit every taste. Come see the **Limestone 24**, our ultimate runabout, the just-launched **Pearson 38** and our complete line of highly finished, highly engineered **Tollycrafts**.

Call or stop by. Yacht Headquarters Bend Boat Basin Portsmouth, RI 02871 **(401) 683-2200.**

There are three ways to bil

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85		Medicare pmt/adj.		-46.-	-8.-	47.-
10/10/85		patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		Pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/Adj		-26.-	-5.-	807.-
1/17/86		court adj.			-3.-	804.-
2/2/86		Medicare pmt/Adj		440.-	250.-	114.-

PLEASE PAY AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS IN YOUR LEDGER CARD

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

AMOUNT REMITTED

James Smith
100 Main Street
Any City, USA

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86
BILLED TO 2-20-86
DATE 2/21/86
ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

our patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Words are *printed.* You're not judged by someone else's scribbles.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

Patient year-to-date payment totals.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A

STATEMENT

FED I.D. #00-0000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	L D C	DESCRIPTION	CHARGES PAYMENTS ADJ PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT						
	YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS	NEW BALANCE	PATIENT	INSURANCE
.00	4.00	.00	.00	.00		4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT NEW BALANCE" SHOWN

STATEMENT DATE	PATIENT PAY Y T D	ACCOUNT NUMBER
02/21/86	.00	12090

LOCATION CODES
1 OFFICE
2 HOSPITAL IN PATIENT
3 HOSPITAL OUT PATIENT
4 OTHER
5 OTHER
6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

This space contributed as a public service.

"YES, THERE IS LIFE AFTER BREAST CANCER. AND THAT'S THE WHOLE POINT."

–Ann Jillian

A lot of women are so afraid of breast cancer they don't want to hear about it.

And that's what frightens me.

Because those women won't practice breast self-examination regularly.

Those women, particularly those over 35, won't ask their doctor about a mammogram.

Yet that's what's required for breast cancer to be detected early. When the cure rate is 90%. And when there's a good chance it won't involve the loss of a breast.

But no matter what it involves, take it from someone who's been through it all.

Life is just too wonderful to give up on. And, as I found out, you don't have to give up on any of it. Not work, not play, not even romance.

Oh, there is one thing, though.

You do have to give up being afraid to take care of yourself.

AMERICAN CANCER SOCIETY®
Get a checkup. Life is worth it.

Created as a public service by Ally Gargano/MCA Advertising LTD.

Some Thoughts on Long Term Care

H. Denman Scott, MD, MPH

Long-term care is a topic which is very important to me. Not too long ago, when I was still in private practice, I came to appreciate the necessity of a well-functioning long-term care system. In fact, I hope to devote a substantial amount of my time as Director of Health to this issue. I would like to share some preliminary perspectives with you. Over the years ahead, I hope you will help to shape my thinking and state policy with respect to long-term care.

Baby Boomers

The long-term care issue is only going to get more attention as time goes along. The post World War II baby boom bulge is currently moving into middle age. In 30 years, when these baby boomers begin to become senior citizens, the percentage of our population 65 years of age and older will increase from about 13 per cent to around 20 per cent. This dramatic increase in the number and proportion of aged people will have a profound impact on the demand for long-term care services. Fortunately, we can see this human tidal wave as it approaches us. We do have time — 30 years — to plan for this demographic challenge. We need to develop a wide array of long-term care services, so we can care for the patient, in the right place, for the right reason, at the right time. In particular, we need to expand our supply of home health services, respite care and especially various forms of congregate living. At the present time, our range of options is too narrow in the long-term care field. The nursing home should be only one of many levels of care within our long-term care system.

Functional Capacity

Long-term care refers to the range of services needed by persons with prolonged or permanent functional incapacities. Such individuals fall overwhelmingly into the older age groups, especially those over 75. All older people in need should have access to an appropriate level of care. The human advantages of home care are obvious to most. Anyone with an intact mind generally abhors the thought of nursing home care and its attendant loss of independence, uprooting, and separation from a setting rich in emotional and physical comforts. Many persons will come to accept the nursing home if they perceive themselves as major burdens to family and friends. Also, a person without family or friends may abandon a home for a nursing home with less functional impairment than a person with substantial family support. As a general rule, the degree of functional impairment should determine the level of care. Home care is the preferred option provided the individual has a home

H. Denman Scott, MD, MPH is Director of the Rhode Island Department of Health, Providence, Rhode Island.

Presented at the Jewish Home for the Aged, Providence, Rhode Island, November 1985.

and someone willing to assume responsibility for his or her care. Institutional care becomes a necessity for many because the extent of impairment overwhelms the human and financial capacity to manage the individual in the home. This situation most commonly occurs in the advanced stages of the dementias, such as Alzheimer's Disease.

Explicit categories of care must be recognized formally. They include medical, nursing, and rehabilitative care. These require special skills. Other categories include personal care as reflected in the ADL (activities of daily living) score, and help with household tasks such as cooking, cleaning, shopping, and handling money. These latter are commonly called the instrumental activities of daily living.

Current Shortcomings

Access to home care is excessively restricted because of reimbursement policies. Medicare (Title XVIII) pays only for "acute therapeutic" care and restricts the number of home care visits by means of strict Utilization Review criteria. Medicaid (Title XIX), while allowing visits for a wide range of problems, restricts the reimbursement rate or payment. The result is that many home care programs, especially those run by the visiting nurse associations, find themselves in serious financial trouble. They are laying off staff and cutting back on these programs.

Eligibility for Medicaid funding is also restricted. A person must be deemed poor, or, in the lingo of the day, "fall below the poverty line." The wealthy have the independence to do as they choose. The near poor are caught in a "Catch 22" bind: too poor to afford care, yet too many resources to be eligible for public assistance. Thus, access to care is not always equitable. Discontinuity of care is another major problem, especially in circumstances where a primary physician can no longer follow the patient or where distance between the primary care physician and the facility is great and makes ready evaluation of the patient difficult. This leads to inefficiency. When a primary physician who knows the patient is not available to evaluate an acute problem, the patient commonly ends up in a hospital emergency room where no one knows his or her past history. An expensive workup often ensues, and important decisions are made without input from family, nurses, or doctors who are familiar with the patient's condition and who also know the patient's wishes about the aggressive or restrained use of medical technology.

Nursing Home Services

Nursing homes must expand their capacity to cope with a variety of acute clinical problems such as various infections, congestive heart failure, and dehydration — to name a few. With augmented clinical skills nursing homes could manage many problems ordinarily handled in hospitals. If we can reduce the number of transfers from nursing homes to hospitals, we can provide more economical and more humane care to nursing home residents. I know from first-hand experience that more definitive medical care can be provided effectively in nursing homes. In order to upgrade the clinical competence of nursing homes, we need a cadre of physicians dedicated to geriatric and long-term care. This is beginning to happen. With an expanding pool of physicians we shall, I predict, see the nursing homes with vastly expanded physician coverage. If this trend is coupled to an upgrading of nursing skills, we shall see a much wider range of care given in the nursing home — provided we can liberate ourselves from rigid (some say constipated) reimbursement policies.

Some Guiding Principles

A long-term care coordinator with a nursing background should determine the appropriate level of care by personal review of an individual's problems. As a general rule, when home care becomes more expensive than institutional care (as it does when 24 hour paid outside help is required), the patient should be placed in an institution. Application of this guideline should not override the principle that placement be primarily based on degree of functional incapacity. Careful monitoring should be carried out to be sure this does not occur.

As in many Canadian provinces, payment should be guided by where the patient is placed. "Spending down" or transferring assets to achieve eligibility, is socially disruptive and often personally traumatic. It should not be allowed to happen.

Government should not bear the entire cost of long-term care. Individuals, except those below the poverty line, should share in the cost. Those persons with higher incomes should assume proportionately greater amounts of the cost than those with modest incomes. All persons should be eligible for some public support. Currently, government supports about 55 per cent of nursing home expenditures. The remainder is paid primarily by individuals. There has been no explicit discussion about what proportion of the

cost government should support. Broad public discussion of this issue is desirable.

Towards the Future

For the elderly, Medicare and Medicaid operate at cross purposes. Medicare aims to reduce acute hospitalization and has little concern about the impact of early discharge on nursing home admissions — since Medicaid pays for most nursing home care. Alternatively, Medicaid is not greatly bothered by hospitalization of the nursing home resident — its sister program, Medicare, generally picks up most of that bill. Both programs, as alluded to earlier, are creating a financial crisis in home care. A common administration and sole-source funding is urgently needed for the acute and long-term care of the elderly. It seems to me highly unlikely that a coherent program will emerge if our current hodge-podge of federal-state approaches continues. Long-term care for the elderly, both institutional and home care, must be dissected from Medicaid, and incorporated into Medicare. An indigent program of medical and long-term care for those under 65 should continue. If these reforms were carried out, means tests could disappear, programs could be established to provide people the proper level of care, and mechanisms could be developed to assure early transition from one level of care to another. Is this a silly pie-in-sky rumination which will only aggravate horrendous budget deficits? I am not sure. I suspect it need not be if proper incentives and utilization review were incorporated. Certainly, significant cost sharing, particularly for long-term care, would be crucial if the bank is not to be broken. How might such a program be structured? It occurs to me that the federal tax reform proposals with only a few brackets, eg, 0 per cent, 15 per cent, 25 per cent, and 35 per cent, could be linked to a reimbursement plan for nursing home and home care services. Those with no tax liability would have no cost-sharing requirement while those in higher brackets would have an increasing obligation. Take, for example, a person needing nursing home care for an indeterminant number of years. In the first year, the individual would have to pay a substantial deductible: eg, 100 per cent for those in the top bracket, 66 per cent for the middle bracket, and 33 per cent for the lower brackets. After the first year, the individual would have a co-payment from 35 per cent to 15 per cent. These percentages could be adjusted to reflect what proportion of long-term care public funds should support. If 50 per cent of the total long-term care bill is the target, this guideline would be given to actuaries for the calculation of deductibles and co-payments. The four bracket system in the tax reform proposal makes this approach relatively straightforward. However, the current 11 bracket system does not preclude application of the basic concept. In any event, I predict that the promise contained in long-term care endeavors will rapidly dissipate unless we establish a coherent, unitary system of finance.

The current system retards innovation. It is obsessed, understandably, with costs. In this obsession, we have lost almost all capacity for flexibility and creativity. Many act as if we have painted ourselves into a corner. Indeed, this may be true. What we must do is run a little risk. Dirty up the paint, buy a new pair of shoes, and get on with initiatives which offer a better future.

A Women's Issue

Finally, let us recognize that about 75 per cent of the people in nursing homes are women. Thus, the issue of long-term care is primarily a women's issue. We can only hope that organized women's groups will take an active interest in the long-term care issue. If this happens, long-term care is more likely to receive the social attention which it deserves.

Conclusion

Let me reiterate that these ideas are preliminary in nature. I want to receive your feedback from the community. With their commitment and help, I am sure that we can fashion a long-term care system that will be beneficial and a source of pride to all Rhode Islanders.

For the business of managing your practice

Workshops:
- **Partnership and Group Practices**
- **Starting Your Practice**

Make a strong start

Entering into private or group practice? Here are two AMA Practice Management workshops designed to help you start out right: *Starting Your Practice*, and *Partnership and Group Practices*. Both feature sound, practical information that you can put to use immediately.

To register for these AMA Practice Management workshops call toll-free: 1-800-621-8335 (Illinois: 312-645-4987.)

Dates and locations of workshops appear below. Both workshops will be offered in Chicago as well. Call the toll-free number above for dates.

From the AMA Department of Practice Management . . . Workshops that work.

Partnership and Group Practices: What You Need to Know Before You Sign a Contract

CONNECTICUT, NEW HAVEN 6/27
MICHIGAN, ANN ARBOR 5/30
NEW YORK, NEW YORK CITY 6/13
RHODE ISLAND, PROVIDENCE 6/27

Starting Your Practice

CONNECTICUT, NEW HAVEN 6/25-26
MICHIGAN, ANN ARBOR 5/28-29
NEW YORK, NEW YORK CITY 6/11-12
RHODE ISLAND, PROVIDENCE 6/25-26

Physician Screening Practices and Colorectal Cancer Screening Prevalance Among the Rhode Island Population

Experience is Comparable to that Reported Nationally

Susan Masterson-Allen, MA
Vincent Mor, PhD
M. Peter Lance, MD

Colorectal cancer is the second most common fatal neoplastic disease in the United States, with an estimated 138,000 new cases diagnosed in 1985 and 60,000 deaths resulting from the disease.[1] The incidence of colorectal cancer is divided approximately equally between men and women, and 93 per cent of colorectal cancers occur in persons over the age of 50.[2] Indeed, because colorectal cancer incidence increases with advancing age, the estimated number of new cases per year is likely to increase over the coming decades as the proportion of the population over the age of 65 continues to grow.

Ms. Susan Masterson-Allen is Project Coordinator, Centers for Gerontology and Health Care Research, Brown University.

Doctor Vincent Mor is Director, Center for Health Care Research, Brown University.

Doctor M. Peter Lance is Assistance Professor of Medicine, Brown University Department of Medicine; Roger Williams General Hospital.

Supported in part by an American Cancer Society Cancer Control Grant #229.

In contrast to the higher mortality rate for patients diagnosed as having late-stage colorectal cancer (approximately 25 per cent relative five-year survival), those diagnosed at an early stage of the disease have a 75 per cent chance of surviving five years or more. Since survival is better for those diagnosed early, it is commonly assumed that increasing the proportion of cases diagnosed early rather than late in the course of the disease will reduce colorectal cancer mortality. Consequently, the goal of many colorectal cancer health promotion campaigns is to increase the proportion of cases of colorectal cancers diagnosed as having local disease. With this goal in mind, the national office of the American Cancer Society (ACS) launched a three-year educational program, "Colorectal Health Check (CHECK)," designed to "increase public awareness and accurate perception" of colorectal cancer, particularly in regard to a recommended schedule for diagnostic testing.[3]

Since 1950, Rhode Island's mortality rate from colorectal cancer has exceeded the national average by 10-15 per cent, causing approximately 400 deaths per year.[4] One possible explanation offered for this high death rate is an excess of late-stage diagnoses due to inadequate diagnostic testing for early colorectal cancer in the at-risk population (adults over 40). Accordingly, in June, 1984 the Rhode Island Division of the ACS announced the initiation of a state-wide CHECK campaign with the following immediate goals: "to significantly increase the numbers of adults reached with educational programs about colon

and rectum cancers at the community level and to provide continuing education programs on the physician's role in early detection" (A.S. Glicksman, CHECK Task Force Chairman, statement on CHECK). The proposed campaign had several goals. Planned interventions included professional education programs, public education programs in the community and the worksite, a mass media health promotion campaign, and an occult blood-screening program.

In response to a need by the scientific and service community to document the effectiveness of such undertakings, a grant was awarded by the American Cancer Society to Brown University to conduct an evaluation of the impact of all components of the CHECK campaign. As part of the evaluation, a random sample survey of Rhode Island's primary care physicians was conducted to determine the pre-campaign level of diagnostic testing for colorectal cancer incorporated in routine medical examinations of the at-risk population (persons over 40). Similarly, baseline measures of the population's knowledge and screening behavior concerning colorectal cancer were secured through a random sample survey of the general public. This paper reports the results of both pre-campaign surveys.

Methodology

Physician Survey. A random sample of primary care physicians drawn from the membership roster of the Rhode Island Medical Society was surveyed in late May, 1985. All physicians whose specialty was listed as Family Practice, General Practice, Internal Medicine, Geriatric Medicine, Gynecology, or Obstetrics-Gynecology were considered eligible. If physicians were listed with a second specialty, they were included, unless that specialty was Oncology, Gastroenterology, or Surgery of any kind. Retired or semi-retired physicians were excluded. A random sample of 148 was drawn from a pool of 366 eligible physicians.

A brief form requesting information concerning specific diagnostic practices was sent to all sampled physicians, along with a letter from the chairman of the Physicians' Resource Committee of the CHECK campaign. Respondents were given the option of returning the completed form to the Center for Health Care Research (CHCR) at Brown University or waiting until CHCR staff called to record the information over the phone.

Survey of the General Public. A random sample survey of the general public was conducted by Alpha Research Associates, Inc. in November, 1984 using random digit-dialing techniques. The sample was stratified by the proportion of the population aged 40 years and older as reported in the 1980 Census in each of five geographic regions in the state: Providence, East Bay, West Bay suburbs, Blackstone Valley, and Washington County/Western Rhode Island. Age and gender controls were enforced such that half of the sample was between the ages of 40 and 64 and half over 64. Each age subsample was controlled for gender at approximately half male and half female.

The survey instrument was based on the American Cancer Society's "CHECK YOURSELF" quiz. Questions were asked measuring respondent knowledge, attitude, and health care behavior, including experience with the three most frequently administered tests for diagnosing colorectal cancer. Demographics collected as part of the survey were the age, gender, level of education, and region of residence of the respondent. The questionnaire was "introduced" to the pre-campaign sample with a neutral question regarding present health status.

Results

Physician Survey. A total of 134 out of a possible 148 physician responses were received (response rate: 90.5 per cent). Seventeen of these responses were not usable for various reasons (eg, doctor performed administrative work only, specialty incorrectly listed). Only 8 physicians refused to participate, and 6 were unavailable. Therefore, results are based on 117 usable responses.

The respondent sample is described in respect to several variables of interest in Table 1. Fewer than 10 per cent graduated from medical school within the past ten years, and 17 per cent graduated before 1945. Fifty per cent of the sample graduated between 1955 and 1974. Half of the respondents specialize in Internal Medicine, while Obstetrics-Gynecology, Family Practice, and General Practice are represented in comparable numbers. Only 6 respondents list their specialty as Gynecology and three as Geriatric Medicine. Three-quarters of the sample are in individual practice, and 16 per cent are in group practice. Only two physicians practice within a Health Maintenance Organization, and another two have both individual practices plus a second type of practice.

Survey results are summarized in Table 2. Sixty-eight per cent of physicians report screening asymptomatic patients over the age of 40. An additional 11 per cent report screening patients over the age of 50. An overwhelming majority

Table 1. Sample Description: Physician Practice Survey (n = 117)

	n	%
Year Graduated Medical School		
1925-34	4	3.4
1935-44	16	13.7
1945-54	21	17.9
1955-64	31	26.5
1965-74	28	23.9
1975-81	11	9.4
Missing	6	5.1
Total	117	100.0
Physician Specialty		
Family Practice	16	13.7
General Practice	12	10.3
Geriatric Medicine	3	2.6
Gynecology	6	5.1
Internal Medicine	59	50.4
Ob-Gyn	21	17.9
Total	117	100.0
Practice Type		
Individual Practice	87	74.4
Group Practice	19	16.2
HMO Practice	2	1.7
Individual and Group	1	0.9
Individual and Other	1	0.9
Total	117	100.0

of the sample perform digital rectal exams (92.3 per cent), and over three-quarters (77.8 per cent) report performing stool guaiac tests as part of their normal practice.

We also sought to determine the extent to which non-specialists performed sigmoidoscopies in their offices rather than referring patients to specialists. Slightly more than one-quarter of physicians sampled (25.5 per cent) report performing proctosigmoidoscopies. Those whose speciality is Internal Medicine were somewhat more likely than other specialties to perform sigmoidoscopies.

Table 2. Physician Practice Survey: Performance of Diagnostic Procedures for Colorectal Cancer (n = 117)

	n	%
Screens asymptomatic patients over forty years of age	80	68.4
Screens asymptomatic patients over fifty years of age	93	79.5
Performs digital rectal exam	108	92.3
Performs stool guaiac test	91	77.8
Performs proctosigmoidoscopy	31	26.5
Number of tests performed in practice		
None	6	5.1
One	22	18.8
Two	59	50.4
Three	30	25.7
Total	117	100.0

Finally, results indicate that fully half of the sample perform two of the three diagnostic tests for colorectal cancer on their patients over 40, and additional 25.7 per cent perform all three tests in their practice. Only 5.1 per cent of physicians sampled do not report routinely performing any tests for colorectal cancer detection.

Survey of the General Public. A total of 1,646 random digit-dialed numbers were called in the pre-campaign survey of the public. Of these, 1,138 reached ineligible parties (non-residences, non-working numbers, no one in residence over the age of 40). An additional 116 parties were not reached, despite a minimum of three call-back attempts. Calls were completed to 745 eligible household members, each of whom was asked to participate in the survey. Two hundred thirty-seven (237), or 32 per cent, refused. Thus, the final sample size of completed surveys was 508.

Table 3. Sample Description: Survey of the General Public (n = 508)

	%
Region of Residence	
Providence	16.3
East Bay	18.9
West Bay	31.1
Blackstone Valley	18.7
Washington County/Western RI	15.0
Gender	
Male	48.8
Female	51.2
Age	
40-54	28.9
55-64	22.7
65-74	31.9
75+	16.5
Education Completed	
Some High School	22.7
High School Graduate	31.3
Some College	11.9
College Graduate	12.7
Post Graduate	7.5
Other	14.0

A description of the sample surveyed is presented in Table 3. Representation by gender is nearly equivalent (49 per cent male vs 51 per cent female). The "oldest old" age category has the lowest representation in this sample (16.5 per cent). The proportion between ages 40-64 is only slightly higher than the proportion aged 65 or over. Rhode Island's five geographic regions are

Table 4. Public Knowledge, Attitude, & Behavior (n = 508)

	%
DO YOU KNOW WHAT COLORECTAL CANCER IS?	
Yes	78.4
No	21.0
Don't Know	0.6
IS THE CHANCE OF GETTING COLORECTAL CANCER HIGHER FOR MEN OR WOMEN?	
Men	22.5
Women	10.7
Same	32.0
Don't Know	34.9
HOW OFTEN SHOULD PEOPLE BE TESTED FOR COLORECTAL CANCER?	
Every 6 Months	20.9
Once a Year	54.2
Every 3 Years	10.6
Every 5 Years	2.0
Less Often Than Every 5 Years	1.0
Don't Know	11.4
DO YOU THINK COLORECTAL CANCER IS CURABLE?	
Incurable	3.7
Curable	82.3
Don't Know	14.0
IF YOUR BOWEL HABITS CHANGED, WHAT WOULD YOU DO?	
See Doctor Immediately	59.3
Wait and Watch	35.3
Ignore It	2.4
Don't Know	3.0
HAVE YOU EVER HAD A DIGITAL EXAM?	
Yes	70.7
No	28.7
Don't Know	0.6
HAVE YOU EVER HAD A PROCTO EXAM?	
Yes	28.2
No	69.0
Don't Know	2.9
HAVE YOU EVER HAD A STOOL TEST?	
Yes	45.9
No	51.6
Don't Know	2.5
HAVE YOU HAD ANY OF THESE TESTS IN THE PAST YEAR?	
Yes	42.8
No	57.2

represented roughly proportionate to population size in these regions. Approximately one-third of the sample (32.1 per cent) had graduated from or at least attended college.

Responses of the random sample to the survey questions are displayed in Table 4. Fully 73 per cent of the sample considered themselves to be in good or excellent health (data not shown). Less than 5 per cent classified themselves as being in poor health.

The majority of the sample (78 per cent) asserted that they know what colorectal cancer is. Thirty-two per cent answered correctly that the chances of getting colorectal cancer are the same for men and women. An equivalent percentage said they did not know the answer (34 per cent). Twice as many respondents thought chances were higher for men (22 per cent) than for women (10 per cent), thus supporting the ACS's opinion that this is a common misconception.

More than half (54 per cent) of the sample answered in accordance with ACS recommendations that people should be tested for colorectal cancer once a year. An additional 21 per cent thought the test should be used more often (every six months). Eighty-two per cent of the respondents answered correctly that colorectal cancer is curable if detected early; less than 4 per cent incorrectly answered that the disease is incurable.

A majority of the sample (59 per cent) indicated an attitude that would positively influence preventive behavior by responding that they would "see a doctor immediately" if they experienced a change in bowel habits, while 35 per cent would "wait and see if problem continued."

The four questions relating to experience with diagnostic testing for colorectal cancer show that 71 per cent of the sample had had a digital rectal examination. Forty-six per cent had had a stool test, but only 28 per cent had ever had a proctoscopic examination. Less than half the sample (43 per cent) had had any one of these tests in the past year.

Discussion

Results of a survey of physician practice patterns indicate an unexpectedly high level of diagnostic testing for colorectal cancer on the part of Rhode Island's primary care physicians, even *before* the onset of CHECK's physician education programs and extensive mass-media campaign. Although it is not clear from this survey whether or not tests are being performed consistently or in accordance with ACS guidelines, it is nevertheless obvious that physicians are substantially sensitized to issues of colorectal cancer detection.

Similarly, results of the survey of the at-risk public indicate a relatively high level of knowledge of the facts of colorectal cancer and a willingness to seek treatment if a symptom of the disease were suspected. Although levels of experience with diagnostic testing do not appear to be particularly high, they are comparable to percentages reported in a national survey of the population over 40 (n = 804) conducted for the national office of the American Cancer Society.[5] The proportions of the Rhode Island and the

national surveys who reported having had a digital rectal examination were exactly equivalent (71 per cent). Proportions reporting ever having had a stool test were very close (Rhode Island, 46 per cent; national, 44 per cent). The largest differential between the two survey populations was in the experience of having had a proctosigmoidoscopy (Rhode Island, 28 per cent; national, 34 per cent), and even in this instance the difference is not great.

In contrasting the physician and public surveys we observe a discrepancy between levels of routine screening practice reported by physicians and levels of screening experience reported by the general public. Some of this difference may be the result of over-reporting by physicians. However, most of the observed differential is probably attributable to two factors: first, not all of the at-risk population receives regular physical examinations and, second, routine screening for colorectal cancer is a phenomenon of recent years which may not be reflected in the proportion of patients who "ever had" one or all of these tests. Nevertheless, the screening experience of Rhode Island's at-risk population is comparable to that reported by a national sample of the same age group, thus suggesting that Rhode Island's elevated mortality rate from colorectal cancer is attributable to some factor or combination of factors other than atypically poor screening practices.

Acknowledgements

The authors would like to acknowledge the efforts of Arvin S. Glicksman, MD, Chairman of the CHECK Task Force and member of the CHECK Evaluation Committee; Frank Cummings, MD, Chairman of CHECK's Physicians' Resource Committee; and Lois Monteiro, Ph.D., Alan S. Morrison, M.D., and Martha W. Turner, all members of the CHECK Evaluation Committee.

References

1. American Cancer Society, Inc. *Cancer Facts and Figures.* New York, 1985.
2. American Cancer Society, Inc. *Colorectal Cancer* (pamphlet). New York, 1983.
3. American Cancer Society, Inc. *Colorectal Health Check Program Guide.* New York, 1984.
4. Buechner, J. S. *Cancer Incidence and Cancer Mortality in Rhode Island 1978-1982: Final Report of the Rhode Island Cancer Information System.* Providence, Rhode Island Health Services Research, Inc., 1984.
5. Shapiro, Leo J. and Associates, Inc. *Cancer of the Colon and Rectum: The Public Perspective. Summary of Findings.* Chicago, 1982.

Centers for Gerontology and Health Care Research
Brown University
Box G
Providence, Rhode Island 02912

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY.... ANYWHERE

PLUS insurance for....
tax audit
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

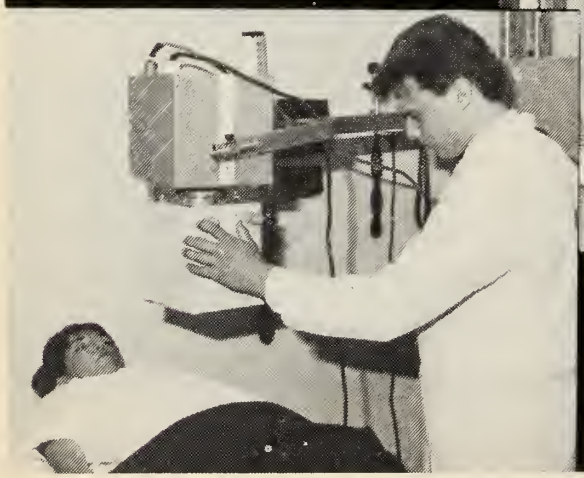
We've become the largest full service medical lab in Rhode Island...*because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

INTERNIST

with an interest in Gastroenterology needed to join a Cardiologist/Internist in a rural Louisiana town from July 1987. Attractive first year salary, benefits, and early partnership.

If interested, send C.V. to:

Manzoor H. Qazi, MD
1101A Port Arthur Terrace
Leesville, LA 71446

Seeking referrals for

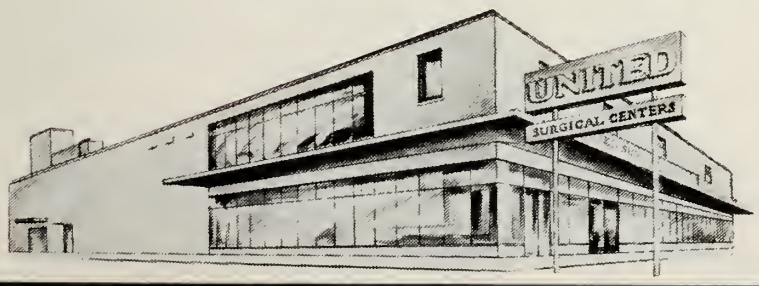
Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

Motrin® 800 mg TABLETS
ibuprofen

Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

News from DISTA about a new dosage form of cephalexin

ANNOUNCING NEW

Keflet™ TABLETS

cephalexin

All the advantages of cephalexin in a convenient tablet form

- Backed by over 15 years of clinical experience
- Smaller tablet is specially shaped and coated for easier swallowing
- May enhance patient compliance, particularly among the elderly
- Tablet dosage form may be appreciated by patients of all ages

NEW Keflet Tablets are available as:

250-mg Tablets

500-mg Tablets

Keflet is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-sensitive patients.

1987 DISTA PRODUCTS COMPANY

Brief Summary. Consult the package literature for prescribing information.

Indications and Usage: Keflet™ Tablets (cephalexin, Dista) are indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Respiratory tract infections caused by *Streptococcus pneumoniae* and group A β hemolytic streptococci (Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Keflet is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of Keflet in the subsequent prevention of rheumatic fever are not available at present.)

Otitis media due to *S. pneumoniae, Haemophilus influenzae,* staphylococci, streptococci, and *Neisseria catarrhalis.*

Skin and skin-structure infections caused by staphylococci and/or streptococci.

Bone infections caused by staphylococci and/or *Proteus mirabilis.*

Genitourinary tract infections, including acute prostatitis, caused by *Escherichia coli, P. mirabilis,* and *Klebsiella* sp.

Note—Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

Contraindication: Keflet is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: BEFORE CEPHALEXIN THERAPY IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS AND PENICILLIN. CEPHALOSPORIN C DERIVATIVES SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS.

SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and the cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both drugs.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics cautiously. No exception should be made with regard to Keflet.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins), therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile.* Other causes of colitis should be ruled out.

Usage in Pregnancy—Safety of this product for use during pregnancy has not been established.

Precautions: *General*—Patients should be followed carefully so that any side effects or unusual manifestations of drug idiosyncrasy may be detected. If an allergic reaction to Keflet occurs, the drug should be discontinued and the patient treated with the usual agents (eg, epinephrine or other pressor amines, antihistamines, or corticosteroids).

Prolonged use of Keflet may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Keflet should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

As a result of administration of Keflet, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy—Pregnancy Category B—The daily oral administration of cephalexin to rats in doses of 250 or 500 mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, fetal viability, fetal weight, or litter size. Note that the safety of cephalexin during pregnancy in humans has not been established.

Cephalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals. Nevertheless, because the studies in humans cannot rule out the possibility of harm, Keflet should be used during pregnancy only if clearly needed.

Nursing Mothers—The excretion of cephalexin in the milk increased up to 4 hours after a 500-mg dose; the drug reached a maximum level of 4 μg/mL, then decreased gradually, and had disappeared 8 hours after administration. Caution should be exercised when Keflet is administered to a nursing woman.

Adverse Reactions: *Gastrointestinal*—Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely. The most frequent side effect has been diarrhea. It was very rarely severe enough to warrant cessation of therapy. Dyspepsia and abdominal pain have also occurred. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity—Allergic reactions in the form of rash, urticaria, angioedema, and, rarely, erythema multiforme, Stevens-Johnson Syndrome, or toxic epidermal necrolysis have been observed. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported.

Other reactions have included genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue, and headache. Eosinophilia, neutropenia, thrombocytopenia, and slight elevations in SGOT and SGPT have been reported.

Pv 2211 DPP [111786]

Additional information available to the profession on request from

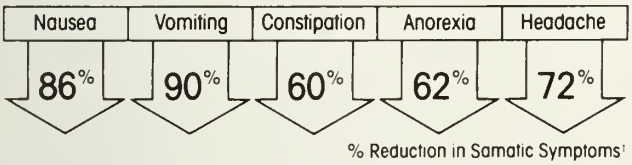
DISTA **Dista Products Company**
Division of Eli Lilly and Company
Indianapolis, Indiana 46285
Mfd by Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

720073

See the difference in the first week[1]

Significantly faster relief—62% of total four-week improvement evident in first week versus 44% with amitriptyline alone[1]

Dramatic first-week reduction in somatic complaints[2]



% Reduction in Somatic Symptoms[1]

Only ⅓ the dropout rate due to side effects of amitriptyline alone, although the incidence of side effects is similar[1]

Caution patients about the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to the lowest effective amount in elderly patients.

Copyright © 1987 by Roche Products Inc. All rights reserved.

Protect your decision. Write "Do not substitute."

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓒ

References: 1. Feighner JP, *et al: Psychopharmacology 61* 217-225, Mar 22, 1979 **2.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ

Limbitrol® Ⓒ
Tranquilizer—Antidepressant

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use, then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single h.s. dose may suffice for some patients. Lower dosages are recommended for the elderly. Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.

How Supplied: *Double strength (DS) Tablets*, white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets*, blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500, Tel-E-Dose® packages of 100, Prescription Paks of 50.

ROCHE®
ROCHE PRODUCTS INC
Manati, Puerto Rico 00701

PI 0585

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

14

Rhode Island Medical Journal

June 1987
Volume 70, Number 6

Doctor Americo A. Savastano, a pioneer in sports medicine, recognized the special needs of youth playing in high school and college athletics

CONTRIBUTIONS

245 Upper Extremity Injuries in Athletes: An Overview

255 Sports Related Knee Injuries in the Pediatric and Adolescent Athlete

265 Rhode Island High School Athletic Injuries 1985-86

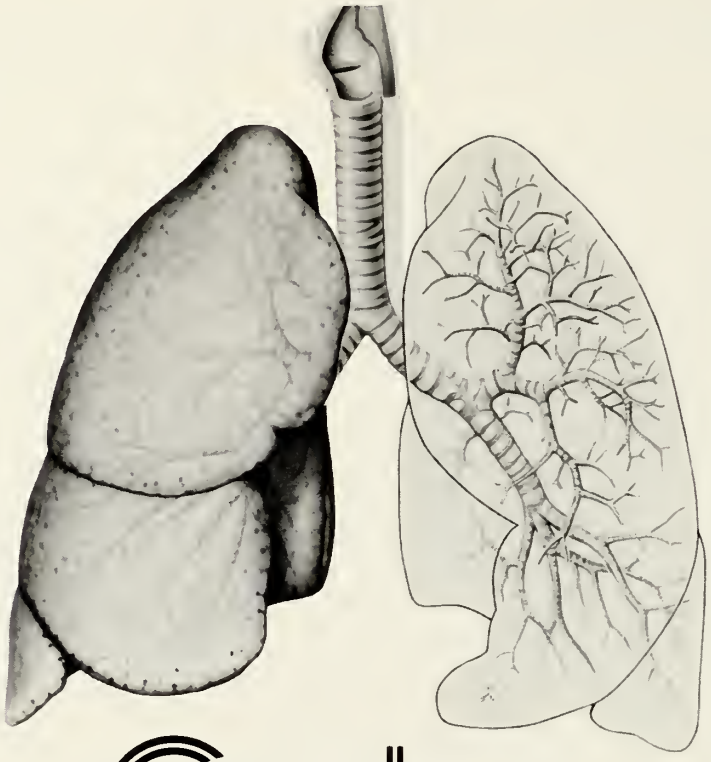
237 EDITORIAL

239 NECROLOGY 1986

251 INFORMATION FOR AUTHORS

272 PERIPATETICS

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, Streptococcus pneumoniae
(ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae,* and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Contraindication:
Known allergy to cephalosporins.

Warnings:
CECLOR SHOULO BE ADMINISTEREO CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS ANO CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY POSSIBLE REACTIONS INCLUOE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)
Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly).

[072886R]

PA 8794 AMP

©1987, ELI LILLY AND COMPANY

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

700241

CONFIRMED

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

JUN 1 -

CONFIRMED BY CLINICAL EVIDENCE

ZANTAC® 150 h.s.

ranitidine HCl/Glaxo 150 mg tablets

EFFECTIVE MAINTENANCE THERAPY

for healed duodenal ulcer patients

See last page for references and
Brief Summary of Product Information.

Glaxo / ROCHE

CONFIRMED

In two randomized, double-blind, and well-controlled clinical trials, ZANTAC 150 mg h.s. significantly superior to cimetidine 400 mg h.s. for maintenance therapy in healed duodenal ulcers.

Percent of patients with observed duodenal ulcer recurrence

		0-4 months	0-8 months	0-12 months	No. patients
USA[1]	ranitidine 150 mg h.s.	9%	14%*	16%†	60
	cimetidine 400 mg h.s.	23%	34%	43%	66
UK, Ireland, Australia[2]	ranitidine 150 mg h.s.	8%‡	14%‡	23%‡	243
	cimetidine 400 mg h.s.	21%	34%	37%	241

*p=0.02
†p=0.01
‡p≤0.004
%=life-table estimates
All patients were permitted prn antacids for relief of pain.

These two trials used the currently recommended dosing regimen of cimetidine (400 mg h.s.) and ranitidine (150 mg h.s.). A comparison of other dosing regimens has not been studied.

The studied dosing regimens are not equivalent with respect to the degree and duration of acid suppression or suppression of nocturnal acid.

The superiority of ranitidine over cimetidine in these trials indicates that the dosing regimen currently recommended for cimetidine is less likely to be as successful in maintenance therapy.

Convenient once-a-night dose with a

low incidence of side effects[3]

Headache, sometimes severe, seems to be related to ranitidine administration. Other side effects have been reported; for a complete listing, see the **ADVERSE REACTIONS** section in the Brief Summary.

No significant interference with the hepatic cytochrome

P-450 enzyme system at recommended doses

ZANTAC 150 mg has no significant drug interactions with theophylline, phenytoin, or warfarin. The bioavailability of certain medications whose absorption is dependent on a low gastric pH may be altered when ZANTAC or other medications that decrease gastric acidity are administered.

Zantac® 150

ranitidine HCl/Glaxo 150 mg tablets

One tablet at bedtime
for maintenance

See next page for references and
Brief Summary of Product Information.

Glaxo / ROCHE®

CONFIRMED

Zantac® 150

ranitidine HCl/Glaxo 150 mg tablets

One tablet at bedtime for maintenance therapy in healed duodenal ulcer patients

References:

1. Silvis SE, Griffin J, Hardin R, et al: Final report on the United States multicenter trial comparing ranitidine to cimetidine as maintenance therapy following healing of duodenal ulcer. *J Clin Gastroenterol* 1985;7(6):482-487.
2. Gough KR, Korman MG, Bardhan KD, et al: Ranitidine and cimetidine in prevention of duodenal ulcer relapse: A double-blind, randomised, multicentre, comparative trial. *Lancet* 1984;ii:659-662.
3. Data available on request, Glaxo Inc.

ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:

1. Short-term treatment of **active duodenal ulcer.** Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD).** Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of therapy.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Although recommended doses of ZANTAC do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Lack of experience to date precludes recommending ZANTAC for use in children or pregnant patients. Since ZANTAC is secreted in human milk, caution should be exercised when administered to a nursing mother.

ADVERSE REACTIONS: Headache, sometimes severe, seems to be related to ZANTAC® administration. Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, premature ventricular beats, and arthralgias. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients.

In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

There have been rare reports of reversible leukopenia, granulocytopenia, thrombocytopenia, and pancytopenia.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Incidents of rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

© Copyright 1983, Glaxo Inc. All rights reserved. October 1986

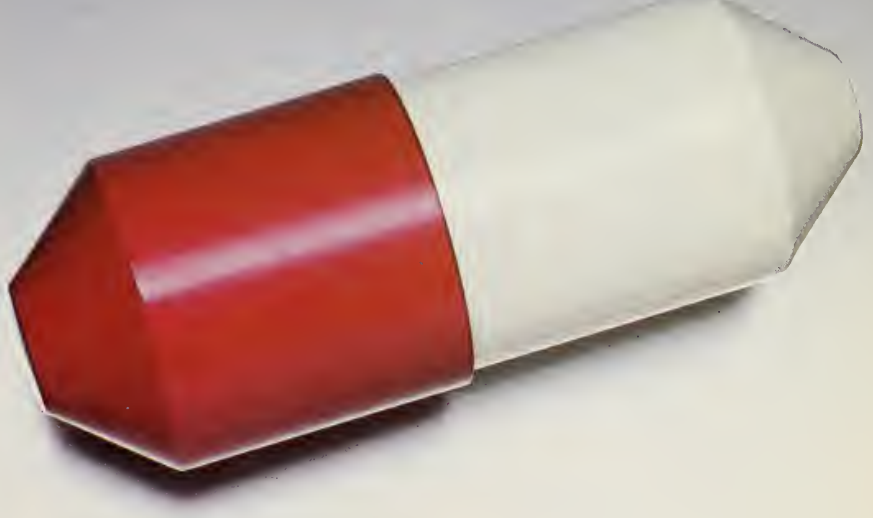
Glaxo

Glaxo Inc.
Research Triangle Park, NC 27709

In Hypertension*... When You Need to Conserve K+

Remember the Unique Red and White Capsule: Your Assurance of SK&F Quality

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).



Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: **Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired.** If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ.L42

Potassium-Sparing

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Over 20 Years of Confidence

The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

a product of

SK&F CO.

Carolina, P.R. 00630

©SK&F Co., 1983

Motrin® 800 mg TABLETS
ibuprofen

Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

Rhode Island Medical Journal

June 1987
Volume 70, Number 6

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Edward R. Feller, MD
Chairman

*Stanley M. Aronson, MD
Contributing Editor

*Maurice M. Albala, MD

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

*John F. W. Gilman, MD

*Edwin J. Henrie, MD

*Toussaint A. Leclercq, MD

Robert V. Lewis, MD

Robert Powel
Student

*Peter L. Mathieu, Jr., MD

*P. Joseph Pesare, MD

*Sumner Raphael, MD

Henry T. Randall, MD

*Guy A. Settipane, MD

*David T. Barrall, MD
Resident

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

SAVE THIS DATE

SIXTH ANNUAL ELLA T. GRASSO MEMORIAL CONFERENCE
November 18, 1987

This symposium addresses current clincial problems in gynecologic oncology and research developments that will impact on patient care. It is directed toward obstetricians/gynecologists, medical oncologists, radiation therapists, pathologists, nurses and residents. The symposium is sponsored by the Divisions of Gynecologic Oncology at the Yale University School of Medicine, the Yale Comprehensive Cancer Center and the University of Connecticut School of Medicine.

Location

The Park Plaza
155 Temple Street
New Haven, CT 06511
(203) 772-1700

Guest Faculty

J. Taylor Wharton, M.D.
M. D. Anderson Hospital and Tumor Institute

Peter Wiernik, M.D.
Montefiore Hospital Medical Care

Richard I. Reid, M.D.
Sinai Hospital of Detroit

Howard W. Jones, III, M.D.
Vanderbilt University Medical Center

Maria Merino, M.D.
NIH — NCI

Jeffrey Schlom, M.D.
NIH — NCI

For registration and further information (after AUGUST 1, 1987):

Yale University School of Medicine
Office of Graduate and Continuing Education
New Haven, CT 06510
(203) 785-4578

TABLE OF CONTENTS

237 **EDITORIAL**

The Benefits and Risks of Physical Exercise

Stanley M. Aronson, MD

239 **NECROLOGY 1986**

272 **PERIPATETICS**

CONTRIBUTIONS

245 **Upper Extremity Injuries in Athletes: An Overview**

Proper Treatment of the Injury Depends Upon Careful Evaluation

Edward Akelman, MD

255 **Sports Related Knee Injuries in the Pediatric and Adolescent Athlete**

Prevention of Injuries in Child Athletes Requires Appropriate Conditioning and Competition Levels, Quality Coaching, and Good Supervision

Ira J. Singer, MD

265 **Rhode Island High School Athletic Injuries 1985-86**

Goal is Improved Injury Prevention Based on These Data

Ernest B. Lowe, Jr., MD
Earle R. Perkins, MS
James H. Herndon, MD

COVER: *Photograph of the late Americo A. Savastano, MD provided courtesy of Mrs. Savastano.*

When you want to maximize the return on your significant income and assets, call a Hospital Trust Private Banker. For maximum strategies for your financial future.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Equal Opportunity Lender

EDITORIAL

The Benefits and Risks of Physical Exercise

Athletics has always played a prominent role in our lives, but until recently we observed rather than participated. Exercise, defined here as planned, structured, and repetitive bodily movement undertaken to improve or maintain one or more components of physical fitness, has now been recognized as medically beneficial. Physical activity, in addition to the personal joy it brings, is clearly of value in aiding weight control, cardiovascular integrity, body sturdiness, and mental health.

These perceived merits of exercise, abetted by a steady increase in available leisure time, has now propelled an increasing fraction of our population into some form of recreational physical activity. Decades ago only the young or middle-aged males regularly participated; currently, the majority of the population engages in some form of exercise, and a jogging grandmother is no longer the object of astonishment. Polls show an impressive increase in the numbers of Americans participating in some form of physical exercise. In 1961, 24 per cent of adults regularly exercised; by 1984, the number had risen to 59 per cent. Indeed, in 1985, over 100,000 Americans had registered for organized marathons.

There are obvious benefits but there are also some new risks. A casual review of some of our professional journals, for example, yields the following list of problems arising during recreational physical activity:

- Hypoglycemia occurs in normal subjects during prolonged exercise and results in an exaggerated rise in plasma epinephrine. (N Eng J Med 306:895, 1982).
- Creatine kinase MB isoenzyme serum concentrations rise during competitive swimming and track racing. Elevations of this isoenzyme, " . . . must be viewed cautiously when the diagnosis of myocardial ischemia is considered in persons who have engaged in vigorous swimming." (N Eng J Med 306:1180, 1982; 305:764, 1981).
- During marathon running, there is a marked elevation in the blood levels of beta-endorphin and norepinephrine. (N Eng J Med 305:467, 1981).
- Jogging occasionally causes acquired nephroptosis. (N Eng J Med 305:590, 1981).
- Jogging may result in radial nerve palsy. (N Eng J Med 305:768, 1981).
- Jogging causes a transitory leukocytosis as well as elevations of C-reactive protein, ceruloplasmin, and fibrinogen. (N Eng J Med 316:223, 1987).
- Bicycling may cause ulnar nerve palsy. (N Eng J Med 301:1397, 1979).
- Unicycling can result in sciatica and dysuria (N Eng J Med 305:231, 1981).
- Each year in the United States bicycling accidents cause approximately 1,300 deaths and 60,000 injuries, particularly in children. The mortality rate in children resulting from bicycle injuries exceeds the cumulative death rates from accidental poisonings, falls, firearm injuries and most major illnesses. Head trauma is the most frequent cause of death in these cases. (Am J Prev Med 2:330, 1986; Am J Pub Health 77:76, 1986).
- Injuries associated with all-terrain recreational vehicles: During a two-year interval, there were

20 deaths and 538 injuries associated with all-terrain vehicles in the state of Alaska. High blood alcohol was frequently an associated finding in such accidents. (MMWR 34:213, 1985).

- Urban-cowboy rhabdomyolysis and associated myoglobinuria: This has also been noted occasionally in persons engaged in military calisthenics, karate kicking and marathon running. (N Eng J of Med 304:427, 1981).

- Lawnmower arm with trauma to the flexor digitorum superficiales. (N Eng J Med 307:1027, 1982).

- Amenorrhea, bone mineral content and bone density in female athletes; decreasing the frequency of osteoporosis-related injuries through diet and exercise. (N Eng J Med 311:1320, 1984; Pub Health Reps. 99:609, 1984).

Injuries, including those associated with sports, represent the leading cause of disability and death in American children. A recent survey of childhood injury in Massachusetts indicates that persons 19 years of age or younger sustained 22.9 injuries requiring medical attention per 100 residents per year. About 18 per cent of these recorded injuries were directly related to sports activity. A more detailed summary according to age and gender may be found below:

Physical Injuries Requiring Emergency Room Care in Massachusetts Children*

	0-5 yrs.		6-12 yrs.		13-19 yrs.	
	Male	Female	Male	Female	Male	Female
all injuries	1986†	1542	2565	1494	3494	1911
sports injuries	18	12	436	249	959	438
% all injuries	0.9	0.8	17.0	16.7	27.4	22.9

* data modified from S. Gallagher et al. Am J Pub Health 74:1340, 1984
† injuries per 10,000 children per year

Despite the undeniable benefits of exercise, the possibility of hazards — some mechanical, some metabolic and some behavioral — must be considered. It is clear that a substantial fraction of childhood injuries are the result of organized or unorganized sports activity. The technical manner by which these injuries are sustained must hence be studied before effective prevention programs may be undertaken. Our knowledge concerning sports medicine remains meager; there is so much to learn as to why only certain amateur athletes sustain injuries; and why, as with vehicular injuries, the distribution of these injuries is so nonrandom. This month's issue of the *Journal* contains three papers by Doctor James Herndon and his associates which begin to address this increasingly important medical issue.

Stanley M. Aronson, MD

NECROLOGY — 1986

William A. Horan, MD
Doctor William A. Horan, an orthopedic surgeon, died January 17, 1986 at the age of 90.

A graduate of Tufts University and Tufts Medical School in 1920, he served an internship at St. Joseph's Hospital and the Hospital for Ruptured and Crippled. Doctor Horan was a private in the U.S. Army Medical Reserve. He was chief of orthopedics at St. Joseph's Hospital from 1934 to 1960, and named chief of staff in 1935. He was appointed head of the crippled children's division of the State Department of Health in 1940, and held that position until 1960. He was surgeon-in-chief of the orthopedic department of the former Charles V. Chapin Hospital.

Doctor Horan was a fellow for the American Academy of Orthopedic Surgeons, and a member of the Providence Medical Association, the Rhode Island Medical Society and the American Medical Association.

Doctor Horan was the husband of Katherine L. Horan.

Parker Mills, MD
Doctor Parker Mills, a Providence physician for 65 years, died January 28, 1986 at the age of 90.

Doctor Mills did an internship at the Jewish Women's Hospital in Boston in 1917 and at the Providence City Hospital from 1918 to 1921. He was a major in the U.S. Army Medical Corps, with the 130th EVAC Hospital during World War II. He earned the EAME ribbon with two battle stars. Doctor Mills was a member of the Providence Medical Association, the Rhode Island Medical Society and the American Medical Association. He was a fellow of the American College of Anesthesiologists.

Doctor Mills was the husband of Dorothy M. Mills.

Rodrigo Rego, MD
Doctor Rego, a Providence physician for 35 years, died January 28, 1986 at the age of 84.

Doctor Rego was a graduate of the University of Lisbon, and interned at the former Union Hospital, Fall River. During World War II, he served in the Army Medical Corps in the European Theater, and was discharged in 1947 with the rank of the staffs of Memorial Hospital and Miriam Hospital. He was a member of the Rhode Island Medical Society.

Doctor Rego was the husband of Jane Rego.

Ernest J. Smith, MD
Doctor Smith, a pioneer in preventive medicine, died February 15, 1986 at the age of 67.

Doctor Smith graduated from Dartmouth College, New Hampshire in 1939 and also Tufts Medical School in 1943. He served an internship and residency at Rhode Island Hospital from 1943 to 1946, and he did a residency at Pawtucket Memorial Hospital from 1946 to 1947.

Doctor Smith earned national recognition in 1963 for conceiving and carrying forward the first community-sponsored measles clinic in the country. In 1966, his work was praised by the late Rep. John E. Fogarty in a speech on the U.S. floor.

Doctor Smith was the husband of Dorothy Smith.

George Meissner, MD
Doctor Meissner, a pathologist-in-chief at Rhode Island Hospital for four years died March 12, 1986 at the age of 70.

Doctor Meissner received his medical degree from Queen's University in Kingston, Ontario in 1943. After his internship in St. Joseph's Hospital in London, Ontario he served until 1946 in the

Royal Canadian Medical Corps as Captain. He served his residency in pathology at the Mallory Institute, now Boston City Hospital. He was a member of several national pathology associations and served twice in 1957 and 1967 as president of the Rhode Island Society of Pathologists.

He was the husband of Betty Meissner.

Edward T. Streker, MD

Doctor Streker, a Providence pediatrician, died March 26, 1986 at the age of 84.

Doctor Streker received his medical degree from Jefferson Medical College, Philadelphia, in 1924. He completed his internship at St. Joseph's Hospital, Providence, and the former Charles V. Chapin Hospital. Doctor Streker was a member of the Providence Medical Association, the Rhode Island Medical Society, the American Medical Association, and the American Pediatric Society.

He was the husband of the late Doris L. Streker.

James W. Lent, MD

Doctor Lent, a general practitioner in Tiverton, died May 18, 1986 at the age of 70.

He was a veteran of the Navy Medical Service, and served from 1942 to 1945. He was a graduate of Rutgers University, New Jersey, and New York City Medical, class of 1933. He was a member of the American Medical Association, the Rhode Island Medical Society, the Fall River and Newport Medical Societies.

He was the husband of Margaret A. Lent.

Jefim Weremchuk, MD

Doctor Weremchuk, a Woonsocket physician, died on May 20, 1986 at the age of 70.

He was educated in the Ukraine and attended medical school at the University of Graz, Austria and received his medical degree in 1952.

Doctor Weremchuk was on the staff of the Woonsocket and Fogarty Memorial Hospitals. He served as a school physician for the city of Woonsocket for approximately 15 years. His membership included the American Medical Association, Rhode Island Medical Society, Ukranian Medical Association of North America and the Woonsocket Medical Society.

Doctor Weremchuk was the husband of the late Martha I. Weremchuk.

Kate B. Breslin-Nettleton, MD

Doctor Kate Breslin-Nettleton died June 26, 1986 at the age of 86. She attended the University of Toronto where she received her medical degree. She did an internship at Women's College Hospital, Canada. Doctor Breslin-Nettleton was a member of the American Medical Association and the Rhode Island Medical Society.

She was the wife of Dan A. Nettleton. Her first husband was the late Dr. Robert H. Breslin.

Peter C. H. Erinakes, MD

Doctor Erinakes died July 1, 1986 at the age of 74.

Doctor Erinakes was former chief of staff of Kent Memorial Hospital and a practicing physician in West Warwick for more than 37 years.

He was a graduate of the Hahnemann Medical College, Pennsylvania, class of 1936. During World War II, he was an officer with the Army Medical Corps and served under General George Patton. He was a founder of the Kent County Memorial Hospital and became its chief of staff from 1961 until 1971. He was a member of the Kent County Medical Society and the Rhode Island Medical Society.

Doctor Erinakes was the husband of Dorothy M. Erinakes.

J. Kenneth Beezer, MD

Doctor Beezer, an obstetrician and gynecologist at Women and Infants Hospital for 30 years died September 19, 1986 at the age of 62.

He graduated from Pennsylvania State University in 1948 and from Temple University Medical School in 1952. He began his internship at Highland Hospital, Rochester, New York in 1952 and completed a residency at Boston City Hospital in 1957. His memberships included the Providence Medical Association, the Rhode Island Medical Society, and the Academy of Obstetricians and Gynecologists.

Doctor Beezer was the husband of Patricia A. Beezer.

Anacleto Berrillo, MD

Doctor Berrillo, a member of the staff at St. Joseph Hospital from 1938 to 1980, died September 30, 1986 at the age of 81.

Doctor Berrillo graduated from the Jefferson Medical College in 1931. He did an internship at St. Joseph Hospital. He served in the Army from 1942 to 1946 in World War II, attaining the rank of Lieutenant Colonel. He was a member of the American Medical Association, the

Rhode Island Medical Society, and the former Mal-Pighi-Medical Society of Rhode Island.

He was the husband of Jane M. Berrillo.

Gustave L. Pozzi, MD

Doctor Pozzi, an East Providence physician for more than 50 years died October 27, 1986 at the age of 81.

Doctor Pozzi was a graduate from the Temple University School of Medicine. He began his medical practice in 1933. He was an advisory member of the East Providence Air Pollution Control Board and the East Providence District Nursing Association. He was a member of the Temple University Associates, the East Providence Knights of Columbus, the Providence Medical Association and the Rhode Island Medical Society.

He was the husband of the late Elizabeth M. Pozzi, R.N.

Thomas Visgilio, MD

Doctor Visgilio, a Westerly physician and medical examiner, died November 17, 1986 at the age of 83.

Doctor Visgilio was a graduate of Hahnemann Medical College in Philadelphia, Pa. He was a former medical examiner for Washington County, he was also chairman of the Westerly School Committee and a member of the Westerly Democratic Town Committee.

He was a member of the American Medical Association, The Rhode Island Medical Society, and the Washington County Medical Association.

He was the husband of Camille P. Visgilio.

Pio Giannini, MD

Doctor Giannini, a Providence physician for over 50 years, died November 18, 1986 at the age of 94.

He completed his medical studies at the Royal University of Naples in 1916 and received the degree of doctor of medicine with a commendation from the Commission of Examiners. During World War I he served as Medical Lieutenant of Troops occupying Albania and Macedonia. He was a member of the American Medical Association, Providence Medical Association, Rhode Island Medical Society, and the Malpighi Medical Society.

He was the husband of Judith Giannini.

Thomas R. Littleton, MD

Doctor Littleton, an ear, nose and throat specialist, died November 20, 1986 at the age of 73.

Doctor Littleton graduated from the Hahnemann Medical College, Philadelphia, and the Episcopal Eye and Ear Hospital, Washington, D.C. He served in the Army Medical Corps in World War II. Doctor Littleton was a member of the staff at Roger Williams General Hospital where he was former chief of the ear, nose and throat unit. He was a member of the Rhode Island Medical Society and the Providence Medical Association.

He was the husband of Marion Littleton.

Arthur C. Gaudreau, MD

Doctor Gaudreau, a Woonsocket obstetrician, died December 10, 1986 at the age of 65.

Doctor Gaudreau received his medical degree from Tufts University Medical School. He did an internship and residency at the Carney Hospital, Dorchester, Mass., the former Charles V. Chapin Hospital, Providence, and St. Margaret's Maternity Hospital, Dorchester. He also did a one-year residency at Woonsocket Hospital. Doctor Gaudreau began his practice in Woonsocket.

A veteran of World War II, he served as a fighter pilot with the Marine Corps until 1946, when he was discharged with the rank of captain.

He was the husband of Walda Gaudreau.

Russell S. Bray, MD

Doctor Russell S. Bray, the first gastroenterologist in Rhode Island, died December 17, 1986 at the age of 83.

A graduate of Jefferson Medical College in Philadelphia, Doctor Bray completed his internship at Memorial Hospital and the Charles V. Chapin Hospital. In 1965, he devised the Bray-Hauser string test for occult blood, which is used extensively today. He was a member of the AMA, RIMS, and the Bristol County Medical Society.

Doctor Bray was the husband of Sylvia E. (Warwick) Bray.

Edmund Billings, MD

Doctor Edmund Billings, a surgeon on the staffs of Memorial Hospital, Roger Williams General Hospital, and Notre Dame Hospital while in private practice, died December 27, 1986 at the age of 64.

A 1945 graduate of Yale University, Doctor Billings received his medical degree from Harvard Medical School in 1947. He also served in the emergency department at Memorial Hospital and was on the faculty of Brown University Pro-

gram in Medicine. He served in the Army Medical Corps in the Korean War. Doctor Billings was a member of the Rhode Island Medical Society, the American College of Surgeons, the Rhode Island Surgical Society, the American College of Emergency Physicians, and past president of the Pawtucket Medical Society. He served on the Impaired Physicians Committee, was a member of the board of directors of Edgehill Newport, was active in the American Cancer Society, and a past president of its Bristol County chapter. He was instrumental in establishing the oncology file for the State of Rhode Island.

Doctor Billings was the husband of Phyllis (Rea) Billings.

Vincent P. Rossignoli, MD

Doctor Vincent P. Rossignoli, a family physician practicing for 50 years in Providence, died December 29, 1986 at the age of 78.

Doctor Rossignoli received his medical degree from Georgetown Medical School in 1932. He was on the staff of St. Joseph Hospital in Providence.

He was the husband of the late Teresa M. (Ciamporcer) Rossignoli.

Are You Concerned About the Competence of a Certain Physician?

If so, the Peer Review Committee on Physician Competency can offer discreet and effective help. A standing committee of the Rhode Island Medical Society since 1985, the Peer Review Committee works in a completely confidential, supportive way to help assure that physicians consistently meet minimum acceptable standards of medical practice. The primary work of the Committee is to help physicians improve the quality of their care through education.

If you know a physician who can benefit from peer education in a particular area of medical practice, please write Dr. William Colaiace, Chairman, Peer Review Committee on Physician Competency, Rhode Island Medical Society, 106 Francis Street, Providence, RI 02906. For more information, call the Society at (401)331-3207. All referrals are held in strict confidence.

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY....ANYWHERE

PLUS insurance for....
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

DOCTORS WANTED

Like the Marines, we are also looking for a few good men (or women). However, we seek Board Certified Physicians, who are particularly proficient in patient history and physical examinations.

Medical Assessment Programs, soon to open a medical facility in Rhode Island, provides comprehensive Independent Medical Examinations for Workers' Compensation, Liability and Bodily Injury patients.

Part-time — We have part-time openings for a half or full day, or a few days per week.

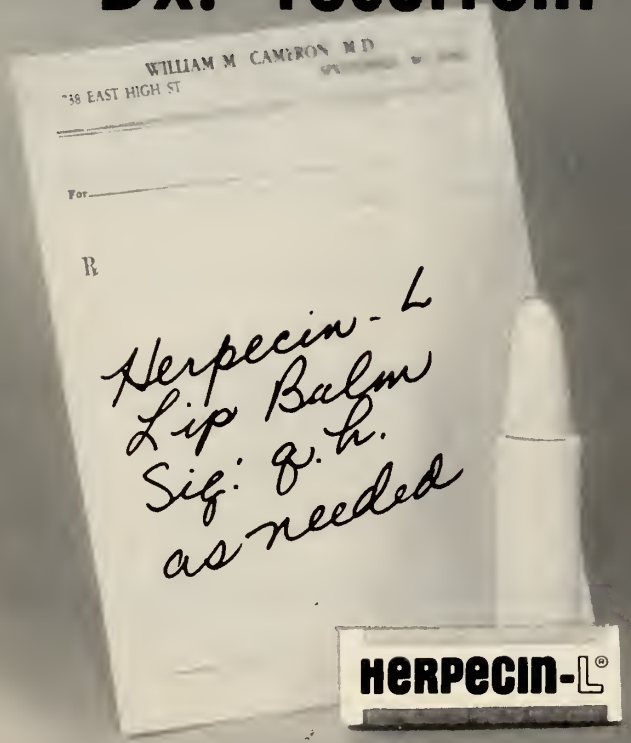
Full-time — According to the Doctor's situation, we have need for a full-time, on staff physician.

Hours are 9 to 5, Monday Through Friday.
Excellent benefits and salary.

For additional information, call Dr. Smith at (617) 449-8201.

Medical Assessment Programs
32 Fremont St.
Needham Heights, MA 02194

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms . . .** blisters **never formed . . .** remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L . .** proven **far superior.**" DDS, PA

"All patients claimed **shorter duration . . .** at **prodromal symptoms . . .** HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for Information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

Upper Extremity Injuries in Athletes: An Overview

Proper Treatment Of the Injury Depends Upon Careful Evaluation

Edward Akelman, MD

Upper extremity injuries in athletes recently have become a focus of increased interest in the medical, orthopaedic, and sports medical literature.[3, 4, 16] This is probably a direct result of the increased numbers of our populace involved in sports, as well as recent developments in understanding the mechanisms of specific injuries in the upper extremity. Proper treatment of these injuries depends on the physician's ability to make a specific diagnosis and to initiate either conservative or surgical treatment plans. Appropriate rehabilitation to return the athlete to either week-end or professional competition is extremely important. This paper presents a review of some of the most common injuries in each area of the fingers and thumb, the hand, the wrist, and the elbow.

Fingers and Thumb

Sports injuries involving the digits and thumb are very common. As distal extensions of the body they are constantly exposed to repetitive trauma, resulting in either minor or major injuries. Most physicians and health care professionals have had the opportunity to examine the patient who complains that he "jammed" his finger or thumb while involved in a sport.[6] Unfortunately, the jammed finger or thumb is a generic term for a complex of injury patterns with either bone, joint, or both bone and joint involvement.[6] Treatment of these injuries is made more difficult because most patients who have sustained these types of injuries think of the traumatic event as a minor one.

As in other fields of medicine, making a specific diagnosis is essential to establish an effective treatment plan. A careful historical review and a complete physical examination is important in helping diagnose these injuries. The single most important diagnostic aid in determining how these injuries should be treated is good radiography. The single most important radiograph is the true lateral film, in which the distal condyles of the proximal phalanx and the middle phalanx are superimposed over one another. Only this x-ray film can help to determine subtle amounts of joint subluxation or bony involvement. Specific injuries can then be diagnosed, with a treatment and rehabilitation plan in mind for each individual patient.

Distal phalanx fractures are usually the result of direct blows. Those fractures that do not involve the articular surface of the distal interphalangeal (DIP) joint are usually treated with simple dorsal splints, which help to protect the tip of the finger as well as to promote fracture healing. When radiographic evidence of healing is seen, the splint can be discontinued. Significant trauma may cause not only distal phalanx fractures, but injuries to the nail matrix as well. If large subungual hematomas are seen during the initial diagnosis and physical examination, the nail matrix should be explored, and repaired if lacerated.

Edward Akelman, MD is an Assistant Professor at Brown University, Surgeon-in-Charge with the Division of Hand and Upper Extremity Service at Rhode Island Hospital and a Consultant at the VA Medical Center, Davis Park, Providence, RI.

Fractures of the middle and proximal phalanx can be managed with conservative methods if they are nondisplaced. Splints are usually used until there is radiographic evidence of healing, and then early mobilization is carried out. Even the smallest proximal phalanx or middle phalanx fracture may cause significant disability by causing decreased range of motion. Proper supervision, using qualified physical or occupational therapists, helps achieve good range of motion and strength in affected digits. Fractures that are significantly displaced, angulated, or rotated require reduction. If the reduction is not readily maintained, percutaneous pinning or open reduction may be required.

Intra-articular fractures of the finger joints cause more difficult management problems. Joint congruity is the single most important aspect in the treatment of these fractures. If a fracture involves a joint but is nondisplaced, simple conservative treatment in a splint with careful follow-up and early mobilization is recommended. If there are large intra-articular fragments, or if the intra-articular fragments are significantly displaced, it is usually recommended that closed reduction and internal fixation using Kirschner (K) wires, or open reduction and internal fixation be carried out. Intracondylar fractures with displacement should also be managed in this way.

Injuries to individual finger joints in sports are common. The so-called "mallet finger," in which either the extensor tendon insertion to the distal phalanx has been ruptured, or a small bony fragment has been pulled off the dorsum of the distal phalanx, is extremely common. This injury can be managed conservatively if a concentric reduction of the joint can be maintained in a splint, or if the intra-articular fragment is smaller than 30 per cent of the joint.[10, 22] If joint congruity cannot be maintained, or if the fragment is too large, the injury should be treated with operative intervention (Figure 1).

The proximal interphalangeal (PIP) joint is the most commonly injured joint in the finger.[6] Such injuries range from volar plate and collateral ligament tears to more complex fracture-dislocation patterns. Treatment is based on physical examination and good diagnostic roentgenographic films (Figure 2). Many PIP joint injuries are overtreated. Most cases of collateral ligament and volar plate injuries are stable. If stability can be demonstrated, splinting of the PIP joint in 20 degrees of flexion for approximately two weeks is sufficient, after which early motion is begun. The use of a border digit for splinting helps maintain normal function. Unstable injuries of the volar plate or collateral ligament complex may require operative intervention.

Fracture dislocations of the PIP joint are difficult management problems.[6, 7, 9, 12, 23, 24] Careful reduction with repeat radiographs combined with dorsal block splinting has been shown to be efficacious.[13] With gross instability, several surgical methods to provide stability have been described.

Dislocations of the metacarpophalangeal (MCP) joint of the fingers and thumb are frequently irreducible.[1, 9] If irreducible, these injuries require open reduction. Early intervention with operative reduction followed by early motion is important in achieving a good post-injury result.

Injuries to the metacarpophalangeal joint of the thumb are seen commonly in sports,[11] more commonly in skiing and gymnastics. A prerequisite for normal pinch and grasp of the thumb is a stable collateral ligamentous complex. This complex can be injured readily if a dynamic valgus stress is placed on the joint.[17] A diagnosis can be made in most cases seen early.[2, 18] A criterion for operative intervention is a thumb metacarpophalangeal joint that does not have a fixed end point on valgus stress, or one in which the joint opens more than 30 degrees. Early operative intervention will provide a better functioning thumb. Injuries that have a fixed end point to a valgus load are treated in a thumb spica cast for approximately four to six weeks.

Hand

The most common sports injuries in the hand proper are metacarpal fractures. Treatment is based on the anatomic location of the fracture.

Intra-articular metacarpal head fractures are most often managed by closed methods. If the fragments are large enough to be held with internal fixation, operative intervention is indicated. Most authors have observed that these fractures are more comminuted than is revealed radiographically, and that open reduction is difficult. Early mobilization is important to maintain optimal functional use of the metacarpophalangeal joint.

Metacarpal neck fractures are usually unstable. Treatment is aimed at achieving a stable reduction. Anatomic reduction in the metacarpals is more important in the index and long metacarpals because of their fixed position in the hand (Figure 3). Slight angulation can be accepted in the border ring and small finger metacarpals, due to their inherent motion. If a stable reduction can be maintained with a cast, this is the

A

B

C

D

Fig 1. This 22-year-old high school baseball player sustained injury to tip of ring finger. A. Note the overlap of the AP x-ray. B. A true lateral shows the joint subluxed and more than one third of the joint surface involved. C. and D. AP and lateral after open reduction.

treatment of choice. If the reduction is not stable, there are several methods available to maintain reduction. Our currently favored method is use of longitudinal K-wires placed through the metacarpal head into the metacarpal shaft. This provides good stability and need be maintained for only approximately three weeks or until healing of the fracture is demonstrated. Active mobilization is then instituted after the Kirschner wire is removed.

Metacarpal shaft fractures result from direct blows or rotational loads. Angulation, or rotation, or both are the most important criteria in determining how these fractures should be treated. Once again, larger angular deformities may be accepted in the ring and small finger

Fig 2. A 27-year-old softball player "jammed" his left index finger playing softball. A. Note that in an AP view of the finger, the index PIP joint appears unaffected. B. A true lateral shows the severity of injury — a fracture, dislocation at the PIP joint. C. After volar plate arthroplasty, a true lateral shows the joint to be well reduced.

metacarpals. Rotary deformities are not acceptable. Nondisplaced fractures can be treated with a cast for four weeks. If there is significant angular or rotational deformity, a stable reduction must be achieved. In some cases this may require open reduction. We currently use percutaneous Kirschner wires to hold an unstable fracture after closed reduction. If reduction is not possible and open reduction is indicated, we sometimes provide rigid stabilization with stainless steel plates and screws. This allows for early mobilization.

A fracture characteristic of sports injuries occurs at the base of the thumb carpometacarpal joint. It is designated Bennett's fracture when the metacarpal has been subluxated proximally, or Rolando's fracture when there is a significant intra-articular component of more than one fragment. These are easily seen with good anteroposterior (AP) and lateral radiographs of the thumb. As both of these fractures are the product of large forces and both are intra-articular, an attempt at that anatomic reduction of the large fracture fragments is important. This can be accomplished either by closed techniques with percutaneous Kirschner wire fixation or by open anatomic reduction with K-wires or small corticocancellous screws. If the fracture is comminuted, closed treatment is indicated. Early mobilization after fracture healing improves thumb function.

Wrist

A common sports injury is the "sprained" wrist. The list of possible diagnoses in such patients is quite large (Table I). Most such injuries are the result of a fall onto an outstretched and dorsiflexed wrist. When initial radiographs show no evidence of a fracture, diagnosing the cause of the pain becomes difficult.

A careful history and physical examination are helpful in the diagnosis. The patient's knowledge of a specific mechanism of injury can point to the anatomic area injured. Point tenderness may be significant. Routine radiographs should in-

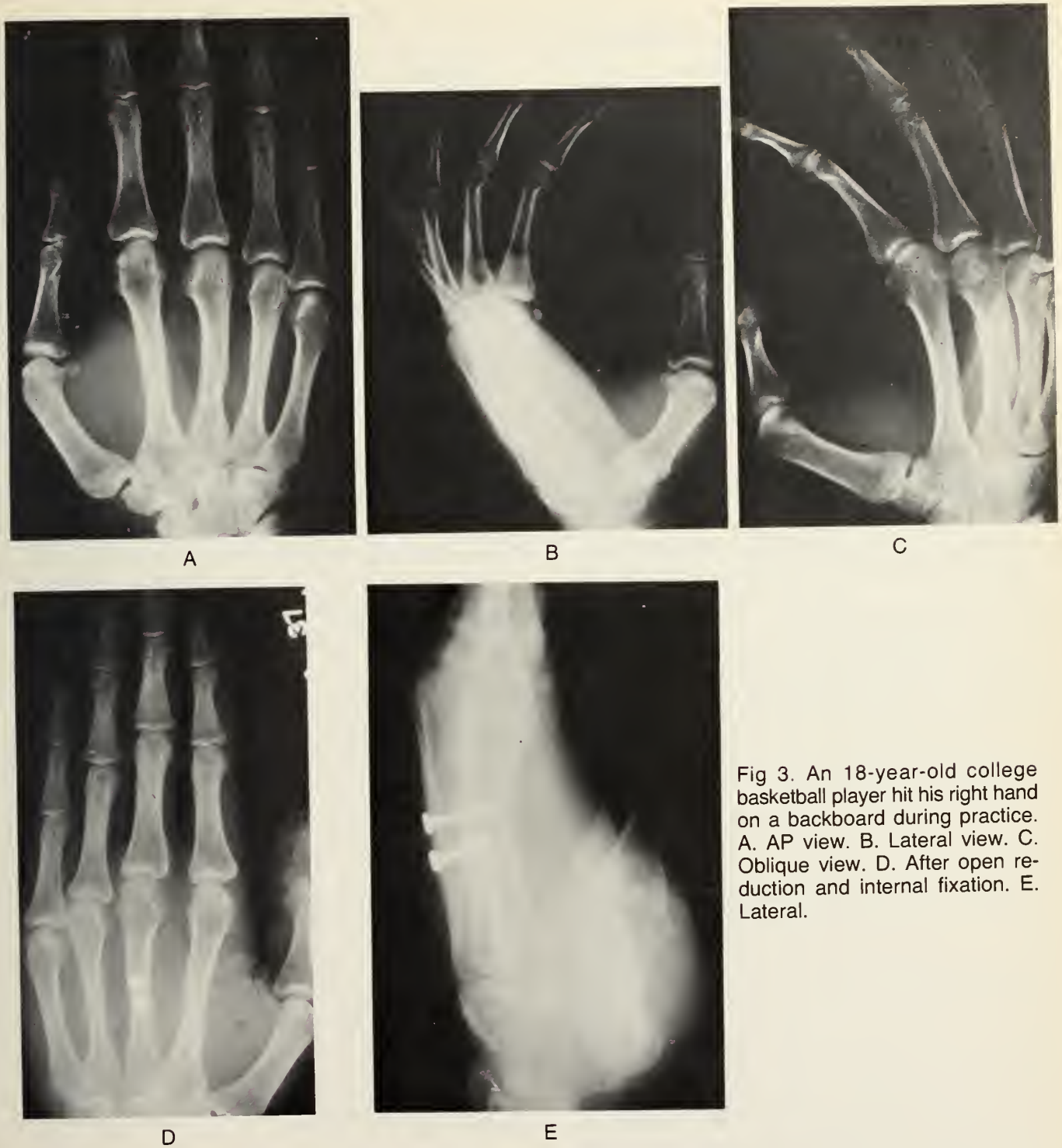


Fig 3. An 18-year-old college basketball player hit his right hand on a backboard during practice. A. AP view. B. Lateral view. C. Oblique view. D. After open reduction and internal fixation. E. Lateral.

clude an AP and a lateral film of the wrist, an AP of the wrist in radial and ulnar deviation, and an AP of the wrist with the patient making a power grip. Instability patterns or other specific injuries may be shown on these x-ray views. Cineiograms, carpal tunnel views, bone scans, arthrograms, polytomography, computed tomography (CT) scans, and arthroscopy may be useful in some cases.

Wrist instability due to rotary subluxation of scaphoid bone is a relatively common sports injury. It is usually caused by a hyperextension injury to the wrist. The usual complaint is of pain and weakness. Tenderness may be elicited in the area of the anatomic snuffbox or between the scaphoid and lunate bones. Diagnosis is confirmed by an AP radiograph when there is a distance of more than 3 mm between the proximal

Table I. "Sprained" Wrist — Differential Diagnoses

Fractures	Diseases	Entities	Instability Patterns
Scaphoid	Keinbock's	Dorsal Ganglion	Rotary Subluxation of scaphoid
Lunate	TFCC tear	Carpal boss	Midcarpal
Triquetrum	Preiser's	DeQuervain's stenosing tenosynovitis	Radiocarpal
Hamate/hook	Radioulnar joint subluxation	Carpal tunnel	Intercarpal
Chondral types	Ulnocarpal impingement	Tendonitis/flexor or extensor	

portion of the scaphoid and the radial portion of the lunate. Lateral radiographs may show increased volar angulation of the scaphoid when compared to the opposite wrist. Simple immobilization or splinting is probably inadequate. In an acute injury careful open reduction of the scaphoid and pinning has been recommended. Most such injuries, however, are diagnosed late after injury. Several types of ligamentous repairs have been proposed for chronic injuries. In long-term follow-up, however, these do not appear to be successful. Watson's scaphoid-trapezoid-trapezium arthrodesis[21] is probably the most effective way to manage this problem, and in follow-up appears to have produced excellent results.[20]

Elbow

The most common elbow condition seen in athletes is lateral epicondylitis, or so-called "tennis elbow." Most patients present with localized pain and tenderness in the area of the lateral epicondyle.[15] The origin of the extensor carpi radialis brevis, the most important wrist extensor, is felt to be the anatomic site of this pain. Microscopic findings of tears in the extensor carpi radialis brevis tendon, as well as immature fibroblastic and vascular infiltrates, have been observed. Careful physical examination usually reveals tenderness just distal and anterior to the lateral epicondyle. Documenting the site of this tenderness is important as proximal diseases such as degenerative arthritis of the cervical spine and thoracic outlet syndrome, and local problems including radial tunnel syndrome have been noted to cause symptoms somewhat similar to lateral epicondylitis, but usually having different anatomic areas of discomfort.

Treatment of lateral epicondylitis is directed at decreasing inflammation at the tendon origin, rehabilitating the muscle, and then changing activity patterns.[14] Treatment in the acute phase, consists of decreased activity, nonsteroidal anti-inflammatory drugs, and a volar cock-up splint. The splint, which decreases the constant pull at the extensor carpi radialis origin, is an important adjunct to treatment. In most cases the pain and discomfort will decrease, but the time required is variable. The goal after pain relief is increasing the strength and flexibility of the flexor musculature of the forearm. Steroid injections are required only occasionally, while surgery in my experience is needed in very few patients.

Our treatment for tennis players follows that initially outlined by Russell Warren.[19] After strength and flexibility is regained, ice on the affected area is recommended for 15 minutes after playing. Lessons may be needed to correct poor technique causing recurrent injury. Racquet alterations may help, using smaller and lighter racquets strung at 50 to 55 pounds tension. Counter-force bracing also appears to have been effective in some patients by decreasing forced transmission through the extensor carpi radialis brevis origin.

Summary

Common sport injuries in the fingers, thumb, hand, wrist, and elbow have been presented. Prompt recognition and specific diagnosis allows for a specific treatment and rehabilitation plan. Treatments should be individualized, with an ultimate goal to return the athlete to his or her previous level of competition.

References

1. Becton JL, Christian JD, Goodwin HN, Jackson JG: A simplified technique for treating the complex dislocation of the index metacarpophalangeal joint. J Bone Joint Surg (Am) 57:698-700, July 1985.
2. Bowers WH, Hurst LC: Gamekeeper's thumb: evaluation by arthrography and stress roentgenography. J Bone Joint Surg (Am) 59:519-524, June 1977.
3. Burton RI: Overview of athleteic upper extremity injuries. In American Academy of Orthopaedic Surgeons: Instructional course lectures 34:297-299, St. Louis, 1985, The CV Mosby Co.
4. Burton RI, Eaton RG: Common hand injuries in the athlete. Orthop Clin North Am 4:809-838, 1973.
5. Coonrad RW. Hooper WR: Tennis elbow: its course, natural history, conservative and surgical management. J Bone Joint Surg 55A:1177, 1973.
6. Eaton RG: The dangerous chip fracture in athletes. In American Academy of Orthopaedic Surgeons: Instructional course lectures 34:314-322, St. Louis, 1985, The CV Mosby Co.
7. Eaton RG, Malerich MH: Volar plate arthroplasty of the proximal interphalangeal joint: A review of ten years' experience. J Hand Surg 5:260-268, May 1980.
8. Froimson AI: Treatment of tennis elbow with forearm support band. J Bone Joint Surg 43B:100, 1961.
9. Green DP, Terry GC: Complex dislocation of the metacarpophalangeal joint. J Bone Joint Surg (Am) 55:1480-1486, Oct 1973.
10. Hammas RS, Horrel ED, Pierret GP: Treatment of mallet finger due to intra-articular fracture of the distal phalanx. J Hand Surg 3:361-363, July 1978.
11. McCue FC, et al: Ulnar collateral ligament injuries of the thumb in athletes. Sport Med 2:70-80, March-April 1974.
12. McCue FC, et al: Athletic injuries of the proximal interphalangeal joint requiring surgical treatment. J Bone Joint Surg (Am) 52:937-955, July 1970.
13. McElfresh EC, Dobyns JH: Management of fracture-dislocations of the proximal interphalangeal joints by extension-block splinting. J Bone Joint Surg (Am) 54:1705-1711, December 1972.
14. Nirschl RP, Petrone F: Tennis elbow: the surgical treatment of lateral epicondylitis. J Bone Joint Surg 61A:832, 1979.
15. Nirschl RP, Stay E: Chapter 28 in Morrey BF: The elbow and its disorders, Philadelphia, 1985, WB Saunders Co.
16. Petrone FA, Ed. Symposium on upper extremity injuries in athletes, American Academy of Orthopaedic Surgeons, 1984, CV Mosby Co.
17. Smith RJ: Post-traumatic instability of the metacarpophalangeal joint of the thumb. J Bone Joint Surg (Am) 59:14-21, January 1977.
18. Stener B: Displacement of the ruptured ulnar collateral ligament of the metacarpophalangeal joint of the thumb: a clinical and anatomical study. J Bone Joint Surg (Br) 44:869-879, November 1962.
19. Warren RF: Symposium on upper extremity injuries in athletes, 233-243, The CV Mosby Company, 1986.
20. Watson HK, Ryu J, Akelman E: Limited triscaphoid arthrodesis for rotary subluxation of the scaphoid. J Bone Joint Surg 68A:345-349.
21. Watson HK, Hempton RF: Limited wrist arthrodesis. I. The triscaphoid joint. J Hand Surg 5:320-327, 1980.
22. Wehbe MD, Schneider LH: Mallet fractures. J Bone Joint Surg 66A:658, June 1984.
23. Wilson JN, Rowland SA: Fracture-dislocation of the proximal interphalangeal joint of the finger: treatment by open reduction and internal fixation. J Bone Joint Surg (Am) 48:493-502, April 1966.
24. Zemel NP, et al: Chronic fracture dislocation of the proximal interphalangeal joint: treatment by osteotomy and bone graft. J Hand Surg 6:447-455, September 1981.

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

There are three ways to bil

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85		Medicare pmt/adj.		-45.-	-8.-	47.-
10/10/85		Patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		Pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/Adj		-28.-	-5.-	807.-
1/17/86		Coord. adj.			-3.-	804.-
2/21/86		Medicare pmt/Adj		440.-	250.-	114.-

PLEASE PAY ANY AMOUNT IN THE OLD MAN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON OUR RECORDS TO-DATE

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86 DATE 2/21/86
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

your patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Words are *printed*. You're not judged by someone else's scribbles.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

Patient year-to-date payment totals.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A

STATEMENT

FED I.D. #00-0000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	LOC	DESCRIPTION	CHARGES PAYMENTS ADJ. PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS	NEW BALANCE	PATIENT	INSURANCE
.00	4.00	.00	.00	.00		4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT" NEW BALANCE" SHOWN.

STATEMENT DATE	PATIENT PAY Y.T.D.	ACCOUNT NUMBER
02/21/86	.00	12090

LOCATION CODES
1 OFFICE 4 OTHER
2 HOSPITAL IN PATIENT 5 OTHER
3 HOSPITAL OUT PATIENT 6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

We've become the largest full service medical lab in Rhode Island...*because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011

CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Sports Related Knee Injuries in the Pediatric and Adolescent Athlete

Prevention of Injuries in Child Athletes Requires Appropriate Conditioning and Competition Levels, Quality Coaching, and Good Supervision

Ira J. Singer, MD

Over the past decade, as the American public has become more involved with fitness activity, there has been a dramatic increase in the participation of children and adolescents in organized competitive athletics. Some estimates state that at any given time 25 per cent of girls and 50 per cent of boys between the ages of 8 and 16 are engaged in competitive athletics in one year.[1] Significant controversy exists about the possible psychological and physiological risks imposed on our children by these new demands, not to mention the possibility of serious injury. Unfortunately research in this field is just beginning to bring forth significant data. Suffice to say, that these young athletes have placed new demands, not only on the orthopedic surgeon, but on pediatricians, psychologists, coaches and trainers.

The significant increase in injuries in these juvenile athletes participating in organized sports is not surprising. In some areas, there has been reported a tenfold increase in the number of these injuries over the past ten years.[2]

Ira J. Singer, MD is an Assistant Orthopedic Surgeon at Rhode Island Hospital and The Miriam Hospital and a Clinical Instructor in Orthopedic Surgery at Brown University, Providence, RI.

As in so-called "free play," acute injuries about the knee resulting from impact or "macrotrauma" are common. Fractures, sprains, and meniscal injuries occur, but whether or not there is a higher incidence of these types of injuries in organized sports, as compared to similar free play activities, has not yet been determined.[2-4] Micheli has repeatedly pointed out that there is a definite increase in the so-called "overuse" types of injuries in children, which is felt to be secondary to "microtrauma." These injuries encompass the soft tissue ailments composed of the bursitides and tendonitides as well as stress fractures, which were once felt to be exclusive in the adult population secondary to repetitive work and weekend sports activities.[5] With the increased emphasis on improving the overall fitness and sports skills of the juvenile athlete, these injuries are being seen in increasing numbers, and in fact it is becoming apparent that the child athlete is probably at greater risk for developing "overuse syndrome." Aside from the usual etiologic risk factors in these situations (training errors, muscle tendon-imbalance, anatomical malalignment, footwear, playing surfaces, and associated disease states), the child is exposed to the so-called "growth factor."[4] The presence of growing cartilage at the epiphysis, at the articular surfaces, and at the apophyseal attachment of major muscle tendon units, seem to put the major joints at

risk for these types of injuries in several ways. Repetitive microtrauma may affect the articular surfaces and growth plates directly, possibly causing growth deformities (genu varum) and even arthritis. The repetitive trauma to these cartilaginous regions has been implicated as an etiologic factor in the osteochondritides as well as the more common Osgood-Schlatter disease.[4,6] Another aspect of the "growth factor" is the growth spurt itself. Due to the longitudinal growth and the secondary elongation of the soft tissues, the resultant incidence in tightness and loss of flexibility of the joints may also predispose to overuse conditions.[7]

The most frequently injured area in childhood and adolescent athletics is the knee.[2] As previously pointed out by Nicholas, the knee is at increased risk because of its exposed position, while providing the essential ability of combined weight-bearing, agility, and locomotion for running and contact sports.[8] The diagnosis of these injuries is, of course, based on obtaining an accurate history and complete physical examination. The nature of the injury, ie, contact or noncontact, weight-bearing status, and time of onset of swelling can often lead the treating physician toward an accurate diagnosis prior to physical examination. The examination should then include assessment of deformity, degree of swelling, ligamentous stability, distal neurovascular status, localization of swelling, and, when possible, range of motion. In the rest of this review, the more common knee injuries in the pediatric and adolescent age group will be presented in terms of their etiology, presentation, diagnosis, and treatment.

Meniscal Injuries

The importance of the fibrocartilaginous meniscus is now well-accepted. Its function as a weight transmitter and stabilizer, as well as a device which aids spreading of the nourishing and lubricating synovial fluid, has been shown by several authors[8-10] (Fig 1). Meniscal tears secondary to shearing forces occur in the adolescent population more often than in younger children. These injuries produce the typical symptoms of tenderness, early and recurrent effusions, and locking. Several authors have pointed out that menisectomy in this age group is not without consequence. Fowler's review shows that 60 per cent of patients 17 years old or younger had difficulty with the affected extremity between 2 and 9 years postoperatively.[9] More recently, Manzione et al showed similarly that 60 per cent of meniscectomized children and adolescents have unsatisfactory results, an average of 5.5 years postoperatively.[11] In view of these statistics, it is important to attempt a conservative approach in such patients and attempt accurate diagnosis utilizing arthrography, arthroscopy, or both to identify the lesion which may lend itself to meniscal repair. Only if the meniscus is unsalvageable should partial meniscectomy be undertaken.[9] Complete postoperative lower extremity rehabilitation is as essential in this age group as it is in the adult population.

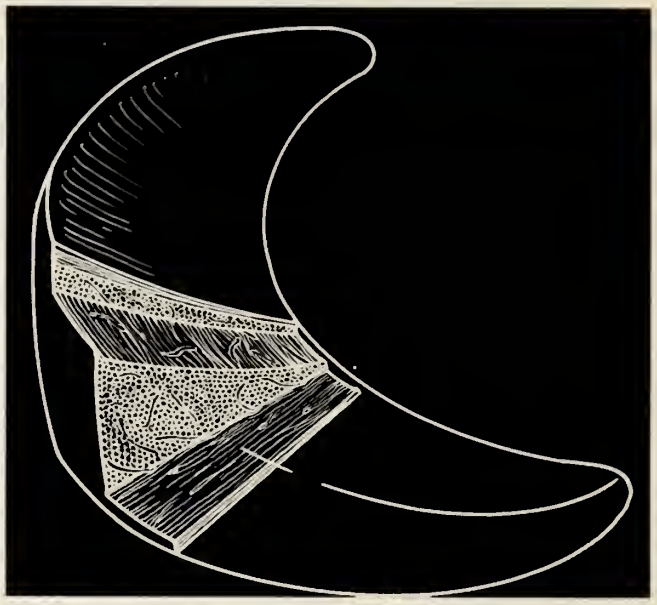
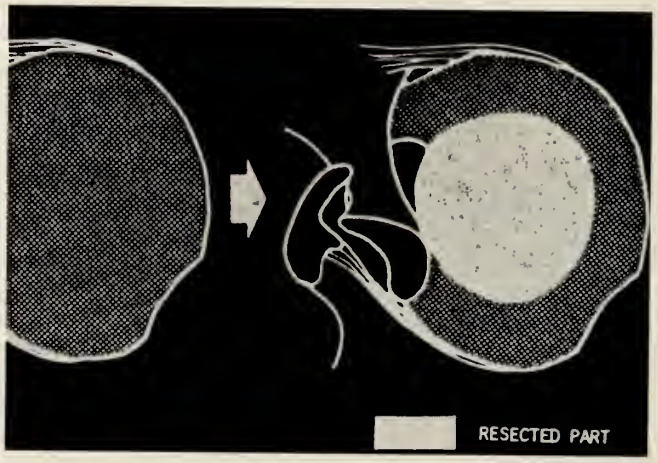


Fig 1. Cross sectional diagram of the meniscus showing orientation of the cartilagenous fibers.[9]

Fig 2. Comparison of pre and post menisectomy shape of the discoid meniscus.[12]



The curious anatomic anomaly known as discoid meniscus is a rare finding, almost always occurring on the lateral side of the joint. Essentially this type of meniscus if felt to be asymptomatic until torn, and it is generally accepted that it suffers a higher incidence of tear than the normal meniscus. The inherent stability of the discoid meniscus is felt to be directly related to the incidence of symptomatic tears. Treatment of the symptomatic lesion consists of arthroscopic partial menisectomy, essentially recreating a semilunar shaped meniscus from the oval disk[9, 12, 13] (Fig 2).

Ligament Injuries

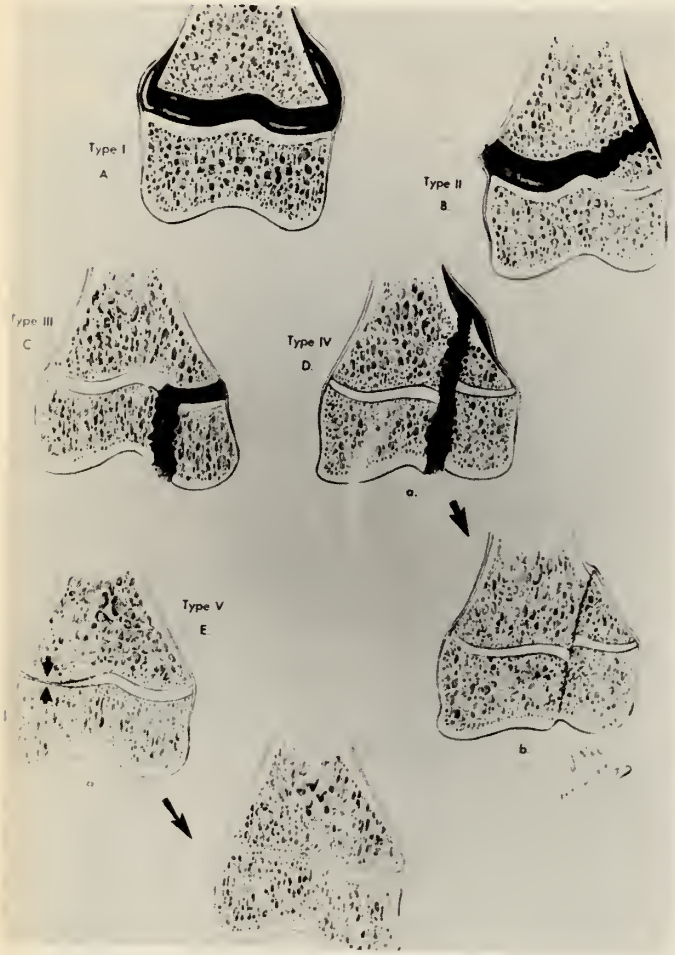
Ligamentous injuries in children and especially adolescents are certainly more common than previously noted.[14] Although the anatomy of the collateral ligaments favors growth plate injuries in this age group, ligamentous disruptions either alone or combined with epiphyseal fractures are well documented and should be considered when confronted with traumatic effusion. This is especially true in avulsion injuries of the tibial spine. Clanton et al showed a high incidence (50 per cent) of tibial spine avulsions accompanied by injury to the tibial collateral ligament.[15] Classically these children present with a swollen knee following a fall from a bicycle.[16] Careful physical examination will usually reveal anterior knee tenderness and medial or lateral tenderness and should lead one to obtain appropriate stress views in order to confirm or rule out associated ligamentous disruptions[16, 17] (Fig 3). Closed reduction under general anesthesia combined with casting is usually successful in obtaining an anatomical reduction of the avulsed tibial spine fragment. However, when associated with collateral ligament injuries, or displacement of the bony fragment, or both, open reduction with repair of the ligament and fixation of the fragment may be necessary. Late instability will lead to a significant number of unsatisfactory results.[15, 18] The rare anterior cruciate injury was recently addressed by Lipscomb et al.[19] In this review 24 patients between the ages of 12 and 15 years were retrospectively reviewed following intra-articular and extra-articular reconstruction for significant anterolateral instability. Twenty-three of the 24 patients obtained good to excellent results at an average follow-up of approximately 3 years. It appears that in this age group failure to diagnose and repair significant anterior or posterior cruciate injuries, either with or without bony avulsion, will lead to late instability. Careful diagnosis and appropriate surgical repair appear to be a preferred course of action for most of these patients.

Fig 3. This 12-year-old child presented with pain and swelling about the right knee following a valgus contact injury. Careful examination and valgus stress testing reveals the Salter I fracture, evidenced by opening of the medial side of the proximal tibial epiphysis.

Fractures

The shearing, avulsion, or impaction injuries that would lead to major ligamentous disruption in skeletally mature individuals are capable of causing epiphyseal separations in the growing child. These epiphyseal injuries are more common than pure ligamentous injuries in children due to the relative weakness of the growth plate compared to the associated ligaments. It should be noted, however, that epiphyseal fractures at the knee are still somewhat rare compared to periarticular fractures through bone only.[20] The Salter-Harris classification (Fig 4) is useful in describing these injuries. The Salter-Harris type II injury of the

Fig 4. The Salter-Harris classification of epiphyseal fractures.



distal femur is the most common of these fractures. Unlike similar injuries at other growth centers, prognosis of the Salter-Harris type II of the distal femur appears to be less favorable.[21] Lombardo's series showed significant (36 per cent) shortening greater than 2 cm over an average four-year follow-up.[22] Czitrom and Salter's series revealed a 1 cm average shortening for similar injuries.[20] In both series, however, the severity of growth disturbance correlated with the amount of initial displacement, the accuracy of final reduction, and those injuries which may have included a crush component (a fall), causing a possible Salter V effect. The Salter-Harris types III and IV afford an even greater chance for shortening and angulation secondary to bony bridge formation and subsequent asymmetric growth (Fig 5). These injuries demand anatomic reduction of both the joint space and when possible the growth plate, in order to minimize growth disturbance and articular incongruity.

Although rare, neurovascular compromise must be excluded in the workup of these injuries. Presence or absence of pulses as well as neurologic deficits must be noted. Arterial injury is somewhat more common in the proximal tibial epiphyseal injuries, especially those involving high impact and subsequent displacement. In the absence of neurovascular deficits, the proximal tibial epiphyseal separations (Salter I and Salter II) usually result in a satisfactory result with appropriate management.[23] More common fractures involving the adjacent metaphyses of the distal femur or proximal tibia can be handled by adhering to standard principles of fracture care. Closed treatment consisting of either casting or skeletal traction is usually sufficient, provided that a reasonable reduction is obtained. In the case

Fig 5. Football injury in a 12-year-old resulted in a Salter IV fracture of the femur, as depicted by the x-ray and intra-operative photo. (Fig 5a and 5b) Open reduction and internal fixation was performed with screws, avoiding the growth cartilage. Rigid fixation allowed early mobilization of this severely injured joint. At 16 month follow up there is no growth deformity.

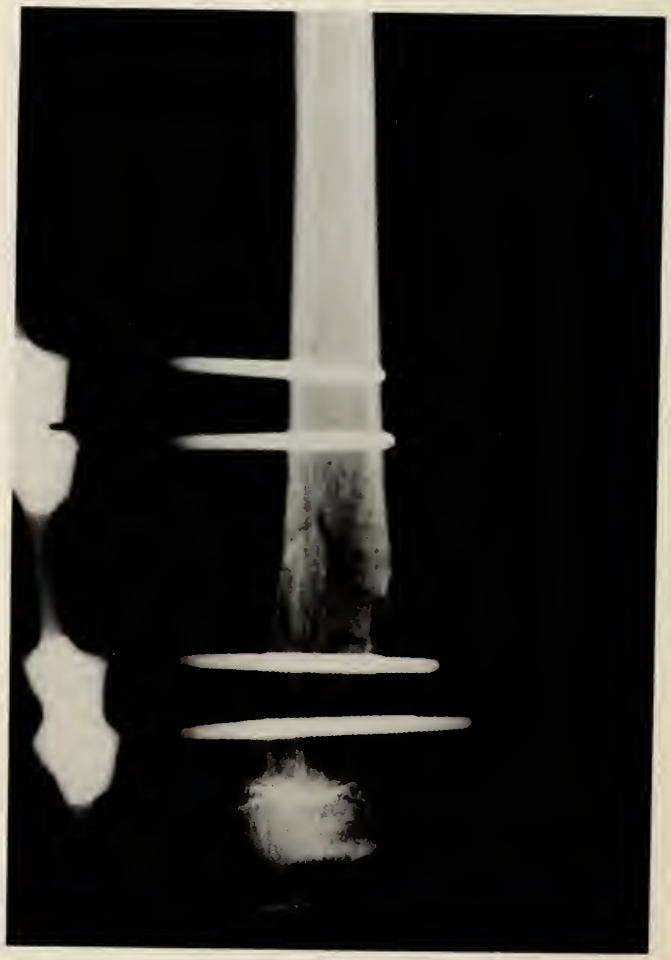
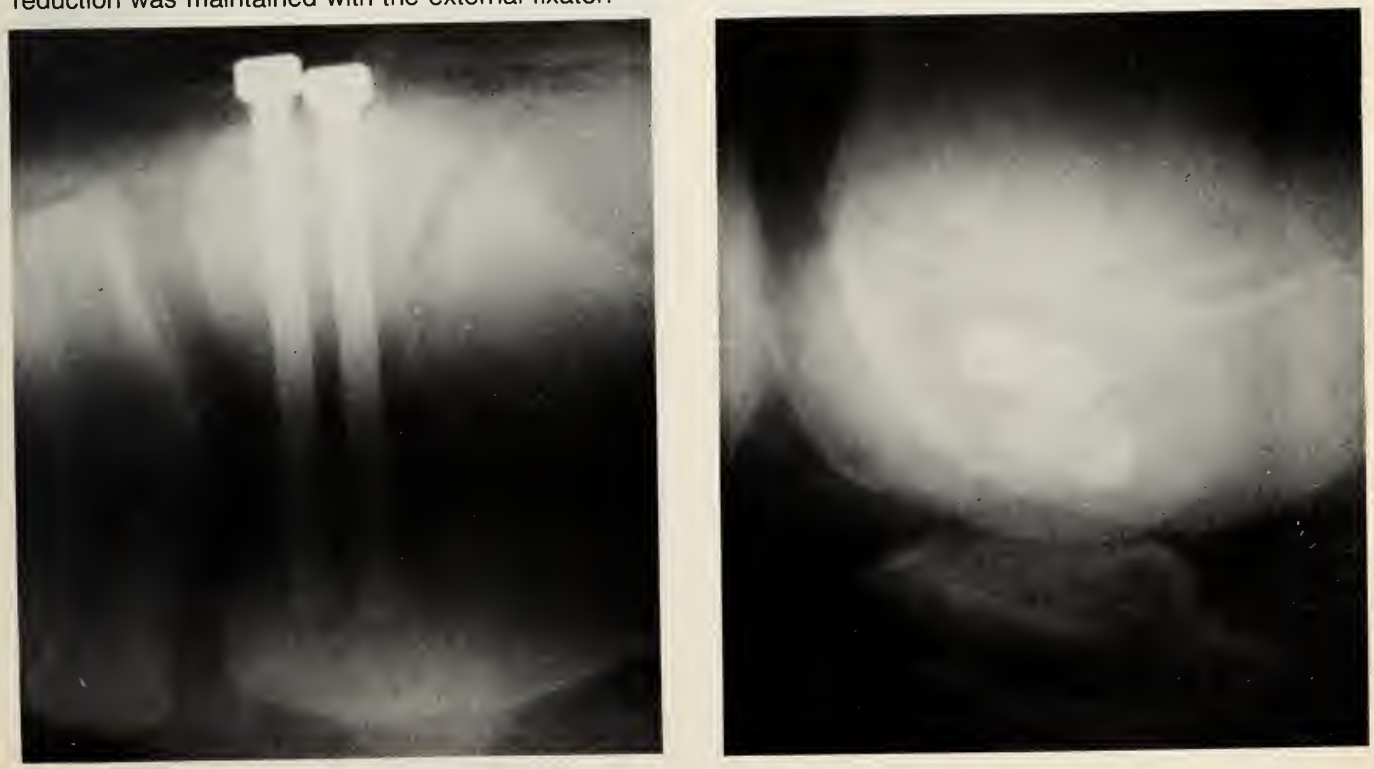


Fig 6. This 12-year-old male sustained a completely displaced supracondylar fracture of the right femur. Anatomic reduction was maintained with the external fixator.



illustrated in Figure 6, a 12-year-old male sustained a completely displaced supracondylar fracture of the femur proximal to the growth plate. It was unreducible in traction, and closed manipulation under general anesthesia failed to gain reduction. Open reduction revealed soft tissue interposition. Reduction was obtained and maintained by the use of an external skeletal fixator.

The common proximal metaphysial fracture of the tibia is well-known to be associated with initial valgus angulation which has been shown to spontaneously correct with longitudinal growth over a 2 to 3 year period.[24]

Acute avulsion of the tibial tuberosity is also a rare injury which is usually seen at the end of the adolescent growth spurt. When this fracture involves displacement of the articular surface of the tibia, accurate reduction and adequate fixation can prevent a poor result. Ogden points out that there is an increased incidence of this fracture when there is evidence of pre-existing Osgood-Schlatter's disease.[25]

Patello-Femoral Pain Syndrome

Pain involving the patello-femoral articulation is an extremely common and difficult problem that confronts the physician dealing with an adolescent athlete. Complaints are often vague and can mimic other knee disorders. It is not at all uncommon to hear complaints of locking, or giving way which may easily confuse the examiner. The pain itself may be related to direct trauma, but far more frequently is the result of an overuse injury to the complex extensor mechanism of the knee. As previously noted, factors such as malalignment (increased quadriceps angle, tibial torsion, foot pronation) and increasing training intensity can lead to significant increases in patellar compressive forces, resulting in pain.[26] The "grinding" pain related to this region is usually aggravated by running, stairclimbing, and sitting in one position for long periods of time (theater sign). It is frequently bilateral. Hungerford described these symptoms accurately as the patello-femoral stress syndrome as opposed to the frequently used term of chondromalacia. The term chondromalacia refers to the specific condition of fibrillation and softening of articular cartilage. This diagnosis, as pointed out by numerous authors, can only be made arthroscopically or histologically. Patello-femoral stress syndromes may eventually cause chondromalacia, but there is certainly no direct relationship between the two events.[4, 27]

Physical examination often will reveal atrophy of the vastus medialis and retropatellar tenderness. A reliable finding is pain with combined patellar compression and quadriceps contraction. Associated findings may include patella alta and an increased Q-angle (quadriceps) which predisposes to lateral patellar tilt or subluxation. The complete knee examination and full radiographic workup including tunnel and skyline views will rule out the other possible diagnosis, including meniscal pathology, ligamentous injury, and occult bone pathology such as tumor or osteochondritis dessicans. One must always consider the possibility of referred knee pain from a primary hip pathology, specifically the slipped capital femoral epiphysis, a growth plate injury (Fig 7).

Fig 7. Typical example of patello-femoral subluxation.

The general treatment of overuse syndromes applies to the treatment of patello-femoral joint problems as well. In this age group, a cornerstone

of therapy, a decreased activity level, is most difficult to achieve. Absolute rest is to be avoided. Methods of decreasing pain include decreasing training routine, altering the training surface, modification of shoe wear including orthotics if necessary, finding alternative forms of conditioning (swimming), and of course quadriceps strengthening and hamstring stretching exercises. Patellar stabilizing braces and controlled doses of anti-inflammatory medication may also be useful. It is generally believed that 90 per cent of patients in this age group will respond to a conservative treatment program as outlined above. Lateral release has been shown to be successful in 65 to 80 per cent of patients not responding to the previously described nonsurgical treatment protocols.[28]

Fig 8. Classic osteochondritic lesion involving the medial side of the medial femoral condyle.

Osteochondritis Dissecans

The etiology of this entity is also widely debated. Direct trauma, malalignment and ischemia have all been implicated by several authors. The possibility that this disease may represent an overuse syndrome has also been proposed. This etiology would correspond well to the associated condition of the capitellum found in the so-called "little league elbow." The name itself is somewhat of a misnomer. While indeed there is a dissected crescentic osteochondral fragment, the underlying pathology itself is not actually an inflammation. The process is most common in the adolescent knee, adjacent to the medial femoral condyle (Fig 8). Pain, swelling, and limitation of motions are usual presenting complaints and may be accompanied by associated quadriceps atrophy. The younger patients tend to have an increased incidence of bilateral involvement and tend to respond well to activity restriction and if necessary a short period of casting. The older group has a higher incidence of frank detachment, which may require excision of the smaller fragments or fixation of the larger lesions that may involve weight-bearing surfaces.[29] In an unpublished report, Litchman et al have successfully correlated viability of the osteochondral fragment with rapid uptake of 99mTc-MDP during arterial phase flow studies, thus providing objective criteria for decision making in the management of this sometimes enigmatic condition.[30]

Osgood-Schlatter Disease

This well-known entity presents an excellent example of "overuse syndrome" in young athletes. Classically confined to boys at the onset of the growth spurt, it is now being seen in female counterparts involved in jumping activities. The large forces of the extensor mechanism combined with the relative overgrowth of the apophysis combine to cause a traction apophysitis. Point tenderness over the tibial tubercle along with enlargement and local swelling are the usual findings. Pain can usually be elicited by forced quadriceps contraction. Activity modification, ie avoidance of jumping and running activities, combined with anti-inflammatory medications and alternative exercise such as biking and swimming, are usually sufficient. Occasionally a separate ossicle may form at the proximal aspect of the tibial tubercle, which has been thought to represent a nonunion of this form of stress fracture (Fig 9). Occasionally, resection of the ossicle and adjacent bursa is necessary and has been reported to relieve symptoms.[31]

Stress Fractures

These overuse injuries are being seen more commonly in the pediatric and adolescent age group. It is well known that these fractures can occur in any bone subjected to repeated cyclical loading and mostly occur in the tibia. Persisent activity-related pain is the hallmark and is usually associated with recent increase in the training program. Point tenderness over a bony surface is often the only hard physical finding. X-ray studies reveal the healing fracture in 50 to 60 per cent of cases (Fig 10).[32] Radionuclide scanning can confirm the diagnosis if there is doubt. Training activities are usually discontinued until complete healing has occurred, in order to prevent a more significant fracture.

Fig 9. This 9-year-old child enjoyed jogging with his father. He was capable of running 2-mile distances several times a week and began developing pain about the proximal tibia. X-ray film reveals the healing stress fracture.

Fig 10. Ossicle formation in Osgood-Schlatter lesion.

Conclusion

Knee injuries in the skeletally immature athlete secondary to either overuse or significant contact trauma are being seen with increasing frequency. Adequate understanding of the anatomic nature of these injuries and their etiologies can aid the physician involved with the care of these patients. Most importantly, injury prevention by appropriate conditioning and competition levels along with quality coaching and supervision should reduce the frequency and severity of these injuries for the child athlete.

References

1. Goldberg, B.: Pediatric Sports Medicine, In Scott Nissenson, and Nicholas (Ed.), Principles of Sports Medicine: Williams & Wilkins, 1984.
2. Micheli, L.J.: Pediatric and Adolescent Sports Injuries: Recent Trends, Exercise Sport Sc Rev, 14:359-374, 1986.
3. Jackson, D.W., Jarrett, H., Baily, D., et al: Injury Prediction in the Young Athlete, A Preliminary Report. Am J Sports Med 6:6-16, 1978.
4. Micheli, L.J.: Overuse Injuries in Children's Sports: The Growth Factor. Orthop Clin North Am 14, April, 1983.
5. Micheli, L.J.: Pediatric and Adolescent Sports Medicine, Boston, MA, Little, Brown, 1984.
6. Ogden, J.A. and Southwick, W.D.: Osgood-Schlatter's Disease and Tibial Tubercle Development. Clin Orthop, 116:180-189, 1976.

7 Guerewitsch, A.D., and O'Neil, M.: Flexibility of Healthy Children. Arch Phys Ther, 25:216-221.
8 Grossman, R., and Nicholas, J.: Common Disorders of the Knee. Orthop Clin of No Am, 8:619, 1977.
9 Fowler, P.J.: Meniscal Lesions in the Adolescent: The Role of Arthroscopy in the Management of Knee Problems, In J.C. Kennedy (Ed.), The Injured Adolescent Knee. Baltimore: Williams & Wilkins, 1979.
10 Nicholas, J.A.: Injuries to the Meniscii of the Knee. Orthop Clin North Am 4:647-664, 1973.
11 Manzione, M., Pizzutillo, P.D., Peoples, A., Schweizer, P.: Meniscectomy in Children: A Long Term Followup Study. Am J Sports Med 11:111-115, 1983.
12 Fujikawa, K., Iseki, F., Mikura, Y.: Partial Resection of the Discoid Meniscus in the Child's Knee. J Bone Joint Surg, 63B-341-395, 1985.
13 Dickhaut, S., DeLee, J.: Discoid Lateral Meniscal Syndrome. J Bone Joint Surg 64A:1068-1073, 1982.
14 Kennedy, J.C.: Ligamentous Injuries in the Adolescent, In J.C. Kennedy (Ed.), The Injured Adolescent Knee, Baltimore: Williams & Wilkins, 1979.
15 Clanton, T.O., De Lee, J.C., Sanders, B., and Neiche, A.: Knee Ligament Injuries in Children, J Bone Joint Surg 61A:1195-1201, 1979.
16 Meyer, M.H., McKeever, F.M.: Fractures of the Intercondylar Eminence of the Tibia. J Bone Joint Surg 52:1677, 1970.
17 Roberts, J.M.: Avulsion Fractures of the Proximal Tibial Epiphysis, In J.C. Kennedy (Ed.), The Injured Adolescent Knee, Baltimore: Williams & Wilkins, 1979.
18 Molander, M.L., Wallin, G., Wikstaaf: Fractures of the Intercondylar Eminence of the Tibia: A Review of 35 Patients. J Bone Joint Surg, 63B: 89-91, 1981.
19 Lipscomb, A.B., Anderson, A.F.: Tears of the Anterior Cruciate Ligament in Adolescents. J Bone Joint Surg, 68A-19-28, 1981.
20 Czitrom, A.A., Salter, R.B., Willis, R.B.: Fractures Involving the Distal Epiphyseal Plate of the Femur. Internat Orthop 4:269-277, 1981.
21 Ehrlich, M.G., Strain, R.E.: Epiphyseal Injuries About the Knee. Orthop Clin of North Am, 10:91-103, 1979.
22 Lombardo, S.J., Harvey, J.P.: Fractures of the Distal Femoral Epiphysis. J Bone Joint Surg 59A:742, 1977.
23 Shelton, W.R., Canale, S.T.: Fractures of the Proximal Tibial Epiphyseal Cartilage, J Bone Joint Surg 61A:167-173, 1979.
24 Skak, S.V.: Valgus Deformity Following Proximal Tibial Metaphyseal Fractures in Children. Acta Orthop Scand 53:141-147, 1982.
25 Ogden, J.A., Tross, R.B., Murphy, M.J.: Fracture of the Tibial Tuberosity in Adolescents. J Bone Joint Surg 62A:205-215, 1980.
26 James, S.L.: Chondromalacia of the Patella in the Adolescent. In J.C. Kennedy (Ed.), The Injured Adolescent Knee. Baltimore: Williams & Wilkins, 1979.
27 Hughston, J.C.: Patellar Subluxation and Dislocation 13-83, Philadelphia: W.B. Saunders Co, 1984.
28 Lankenner, P.A., Micheli, L.J., Clancy R.: Arthroscopic Percutaneous Lateral Retinacular Release, Am Journ Sports Med, 14:267, 1986.
29 Roberts, J.M.: Osteochondritis Dissecans, In J.C. Kennedy (Ed.), The Injured Adolescent Knee, Baltimore: Williams & Wilkins, 1979.
30 Litchman, H.L.: Computerized Blood Flow Analysis for Decision Making in the Treatment of Osteochondritis Dissecans, Presented at the Combined Italian Orthopedic Association and American Orthopedic Association Meeting, Milan, Italy, May, 1986.
31 Mital, M.A., Matza, R.A., Cohen, J.: The So-Called Unresolved Osgood-Schlatter's Lesion, J Bone Joint Surg, 62A:732-739, 1980.
32 Harvey, J.S., Overuse Syndrome in Young Athletes, Clin in Sports Med 2:595-607, 1983.

160 Wayland Avenue
Providence, RI 02906

Presenting...

VALUEplus

A new single premium variable life policy that offers investment opportunity through a choice of ***five*** popular options including zero coupon bonds—and guaranteed lifetime insurance protection.

PLUS...

- 100% tax-free asset accumulation
- Flexibility to move your investment as your needs or market conditions change
- Ready access to your funds
- Income tax-free transfer to heirs

ValuePlus offers you a way to plan for your own financial future and the future security of your heirs. It also provides the potential for substantial growth based on the performance of the funds you select. And...because ValuePlus is life insurance...***your investment grows on a tax-free basis.***

For a prospectus on ValuePlus containing more complete information, including all charges and expenses, mail the coupon below or call (phone number).

ValuePlus is issued by The Guardian Insurance & Annuity Company and distributed by Guardian Investor Services Corporation, both wholly owned subsidiaries of The Guardian Life Insurance Company of America

MAIL TO: **William C. Martin**
Second Vice President

Shearson Lehman Brothers Inc.
180 Westminster Mall, 2nd Fl.
Providence, RI 02903

401 272 1160
1 800 556 7362 Toll Free #

☐ Please send me additional information and a prospectus on ValuePlus. I'll read the prospectus carefully before I invest.

Name

Address

City State Zip
( ) ( )
Business Phone Home Phone

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

There must be a good reason why

UNITED SURGICAL CENTERS

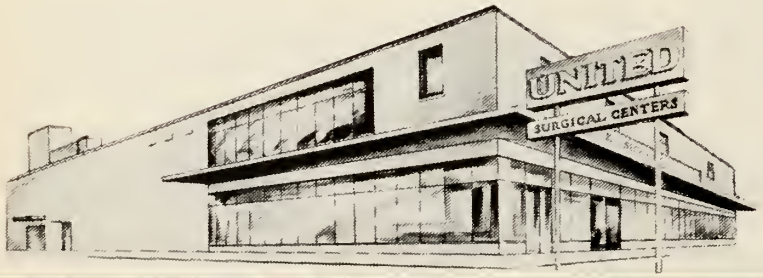
The Professionals in Home Health Care Equipment

we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.



(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

Rhode Island High School Athletic Injuries 1985-86

Goal Is Improved Injury Prevention Based on These Data

Ernest B. Lowe, Jr, MD
Earle R. Perkins, MS
James H. Herndon, MD

Athletics has become an integral part of high school life. It is well known that there are numerous physical, social, and psychological benefits derived from sports participation. With increased participation in sports, however, the chance for injuries also increases. With a grant from the Rhode Island Foundation, a study of Rhode Island Interscholastic injuries was carried out during the 1985-86 school year to determine the frequency of sports-related injuries in our community. Our hope is that by identifying these injuries, appropriate preventative measures can be implemented.

Ernest B. Lowe, Jr, MD is an Assistant Clinical Professor at Brown University Program in Medicine and Surgeon-in-Charge with the Division of Sports Medicine, Rhode Island Hospital, Providence, RI.

Earle R. Perkins, MS is the Coordinator for the Sports Medicine Facility at Rhode Island Hospital, Providence, RI.

James H. Herndon, MD is Professor and Chairman for the Department of Orthopaedics at Brown University Program in Medicine and Surgeon-in-Chief with the Department of Orthopaedics and Rehabilitation, Rhode Island Hospital, Providence, RI.

Supported by a grant from the Rhode Island Foundation.

Methods

During the 1985-86 school year, the A.A. Savastano Sports Medicine Clinic at Rhode Island Hospital recorded and evaluated all injuries occurring in athletics at ten area high schools. These schools represented a geographical cross section of the state as well as all classes of competition. The data were gathered by weekly questionnaires completed by the coaching or training staffs of the various schools. Data likewise were gathered and confirmed through periodic phone calls and on-site visits by our clinic's trainer.

A questionnaire was completed on any participant sustaining an injury which caused the player to miss an organized practice or game. The injury rate was the total number of injuries per total number of participants. In addition, the location, type (ie strain, sprain, fracture, bruise laceration, abrasion), and time (ie practice, game, or other) of each injury was recorded. The questionnaire provided space for comments and evaluation of the severity of a specific injury (Table I).

Table I

AA Savastano
Sports Medicine Center
Rhode Island Hospital

Injury Registry Report Date: _____.

Name of School: _____. Name: _____.

Sport(s) Reporting On: _____. Position: _____.

INJURY: _____ Right _____ Left Sex: _____ Male _____ Female

LOCATION:

_____ Facial
_____ Foot/Feet
_____ Ankle
_____ Lower Leg
_____ Knee
_____ Thigh
_____ Hip
_____ Abdomen
_____ Chest
_____ Shoulder
_____ Upper Arm
_____ Elbow
_____ Lower Arm
_____ Wrist
_____ Fingers
_____ Spine
_____ Neck
_____ Head

TYPE:

_____ Strain
_____ Sprain
_____ Fracture
_____ Bruise
_____ Laceration
_____ Abrasion

SPECIFICS:

_____ Pre-Season
_____ Practice
_____ Game
_____ Contact
_____ Non-Contact
_____ Night
_____ Day

WEATHER:

_____ Sun
_____ Rain
_____ Snow
_____ Indoors

Specific Injury:

Comments:

Results

One-hundred-and-ninety-four injuries were recorded during the 1985-86 academic year. Each participating school reported total participants, allowing us to determine injury rates for each sport (Table II). Obviously, football was the sport in which participants were most often injured. Other "at risk" sports were hockey and soccer.

The locations of the injuries are listed in Table III. The athletes' ankles were the most commonly affected site with knee injuries and hand injuries the next most commonly recorded injuries. Table IV lists the injury types. A sprain, defined as a ligamentous injury to a joint, was the most common. Fractures were second, followed by contusions. Most injuries occurred with contact either during practice or during a game (Table V). Table VI lists severe injuries, which includes any injury resulting in more than two weeks of lost competition. Of forty severe injuries, twenty-four occurred in football (60 per cent). A majority of severe injuries were acute fractures (55 per cent). In the running sports "severe injuries" were stress fractures related to overuse. It is significant that, with football excluded, females had more severe injuries than males (Table VII). This is believed to be secondary to lack of year-round participation and conditioning. The female athletes were also very competitive, adding to their risks. Severe injuries in soccer were second in number to those in football. The goalie in soccer accounted for three of the five severe soccer injuries.

Football injuries are recorded according to player position in Table VIII. Players on offensive units had more than twice as many injuries as the defensive players. Individuals who handle the ball, such as backs and receivers, were most commonly injured. Defensive lineman were, surprisingly, the fourth most commonly injured in this study.

Table II. Total Sports — Total Athletes

Sport	Male	Female	# Inj.	% of 194	Total Male Athletes	Male % Injured	Total Female Athletes	Female % Injured	Total Athletes	Sport % Injured
Football	114	0	114	58.76%	355	32.11%	0	0.00%	355	32.11%
Soccer	19	8	27	13.92%	224	8.48%	68	11.76%	292	9.25%
Basketball	5	8	13	6.70%	215	2.33%	149	5.37%	364	3.57%
Wrestling	9	0	9	4.64%	213	4.23%	0	0.00%	213	4.23%
Track & Field	3	2	5	2.58%	279	1.08%	167	1.20%	446	1.12%
Volleyball	0	5	5	2.58%	0	0.00%	175	2.86%	175	2.86%
Field Hockey	0	4	4	2.06%	0	0.00%	83	4.82%	83	4.82%
Softball	0	3	3	1.55%	0	0.00%	169	1.78%	169	1.78%
Cross-Country	2	1	3	1.55%	125	1.60%	63	1.59%	188	1.60%
Baseball	3	0	3	1.55%	256	1.22%	0	0.00%	246	1.22%
Ice Hockey	5	0	5	2.58%	57	8.77%	0	0.00%	57	6.77%
Indoor Track	1	0	1	0.52%	177	0.56%	13	0.00%	190	0.53%
Tennis	0	1	1	0.52%	105	0.00%	53	1.89%	158	0.63%
Conditioning	1	0	1	0.52%	1	100.00%	0	0.00%	1	100.00%
	162	32	194	100.00%	1997		940		2937	

Discussion

An attempt has been made to record athletic injuries in the Rhode Island Interscholastic League. The schools' personnel were extremely helpful in participating and in completing the injury reports. One-hundred-and-ninety-four injuries were recorded for 2937 athletes participating at the schools for an overall injury rate of 6.6 per cent. Football had the highest injury rate at 32.11 per cent. Similar studies in North Carolina[1] and Spokane, Washington[2] revealed injury rates of 48 per cent and 14.3 per cent respectively.

The second highest injury rate was in soccer (both male and female). The injury rate in females was 9.25 per cent and males 8.48 per cent. A similar study by McCarroll in Indianapolis for a similar age group of males reported an injury rate of 8.74 per cent.[3] Similarly, Grana concluded from his injury registry in Oklahoma that the male and female injury rates were similar for similar sports.[4] Grana's data for basketball injuries are also similar to our overall injury rate of 3.57 per cent. It is difficult to interpret our hockey and wrestling results. A study from Buffalo, NY reported an injury rate of 80 per cent, but included primarily facial lacerations.[5] Facial lacerations not severe enough to result in two weeks' loss of competition did not show up in our study. Also unexplained in this study is a low incidence in wrestling of 4.23 per cent.[6] More detailed studies of these two sports are planned.

The location of injuries is of interest. Football as expected as a rough tackling sport had 47.8 per cent of its injuries located in the lower extremities. Similarly, Mueller[2] in North Carolina (46.2 per cent) and Olson[1] in Spokane (58.2 per cent) found the lower extremity vulnerable. This study reported a 12 per cent incidence of hand injuries which is slightly higher than either North Carolina's (8.0 per cent) or Spokane's (8.17 per cent). Rhode Island high school athletes should have protective taping or padding of their hands to decrease the number of hand injuries.

Soccer and basketball injuries were predominantly in the lower extremity. A soccer lower extremity injury rate of 65.5 per cent was similar to the soccer studies in Indianapolis[3] (58.6 per cent). Injuries in the other running and jumping sports, such as basketball, track, volleyball, and cross country are predominantly to the lower extremities. Upper extremity injuries were commonly secondary to throwing (baseball, javelin) or catching (baseball, basketball) or blocking a ball (soccer).

A sprain or ligamentous injury was the most common type of injury in high school sports. Fractures in this study were secondary to contact and comprise 20.1 per cent of the injuries and 21.0 per cent of all football injuries. Mueller's study records an incidence of fracture of 10.6 per cent in football.[1] Fractures accounted for 22.2

Table III. Injury By Location

	Face	Foot	Ankle	Lower Leg	Knee	Thigh	Hip	Chest
Football	2	4	17	4	16	10	4	4
Soccer								
(M)	2		5		4	1	1	1
(F)			5	2			1	
Basketball								
(M)			2			1		1
(F)	1		2		1	1		
Wrestling			2	1				1
Track & Field								
(M)				2		1		
(F)					1			1
Volleyball			1	1	2			
Field Hockey		1	1	1		1		
Softball		2				1		
X-Country								
(M)			1	1				
(F)				1				
Baseball	2							
Hockey	2				1			
Tennis								
(M)								
(F)			1					
Totals	9	7	37	13	25	16	6	8

Table IV

	Strain	Sprain	Fracture	Concussion	Bruise	Laceration	Abrasion
Football	20	30	24	11	19	2	
Soccer							
(M)	2	7	4	2	9	1	
(F)		5	2		1		
Basketball							
(M)	2	3					
(F)	1	5	1			1	
Wrestling	1	4		1	3		
Track & Field							
(M)	3	1					
(F)	1				1		
Volleyball	1	3			1		
Field Hockey	1		2		1		
Softball	1		1		1		
X-Country							
(M)		1	1				
(F)			1				
Baseball		1	1			1	
Hockey			1		2	2	
Tennis							
(M)							
(F)			1				
Totals:	33	68	39	14	33	7	

Table III. Injury By Location

	Shoulder	Elbow	Lower Arm	Wrist	Fingers	Spine	Neck	Head	Total
Football	10	7	1	1	14	7	3	11	115
Soccer									
(M)				1	2			2	19
(F)									8
Basketball									
(M)							1		5
(F)					2	1			8
Wrestling	3				1			1	9
Track & Field									
(M)		1							4
(F)									2
Volleyball					1				5
Field Hockey									4
Softball									3
X-Country									
(M)									2
(F)									1
Baseball		1							3
Hockey	1			1					5
Tennis									
(M)									0
(F)									1
Totals	14	9	1	3	20	8	4	14	194

Table V. Injury By Condition

	Contact	Non-Contact	Practice	Game
Football	105	10	65	50
Soccer				
(M)	13	6	6	13
(F)	2	6	4	4
Basketball				
(M)	1	4	1	4
(F)	3	5	4	4
Wrestling	7	2	5	4
Track & Field				
(M)		4	3	1
(F)	1	1	2	
Volleyball	2	3	3	2
Field Hockey	2	2	3	1
Softball	1	2	1	2
X-Country				
(M)		2	2	
(F)		1	1	
Baseball	2	1	2	1
Hockey	5		3	2
Tennis				
(M)				
(F)		1	1	
Totals	144	50	106	88

Table VI. Severe Injuries

24	Football	
	1) Fractures	15
	Hand	4
	Clavicle	3
	Ankle	3
	Ribs	2
	Elbow	1
	Forearm	1
	Metatarsal	1
	2) Knee Ligaments	4
	3) Back strain	2
	4) Concussion	2
	5) Shoulder dislocation	1
5	Soccer (Men)	
	1) Fractures	2
	Hand	1
	Ankle	1
	2) Knee ligaments	2
	3) Face	1
	*3 Goalkeepers	
	knee	
	hand	
	face	
1	Soccer (Female)	
	1) Stress fracture — tibia	
3	Basketball (F)	
	1) Hand Fracture	
	2) Stress fracture-tibia	
	3) Ankle sprain	
2	Track & Field (Female)	
	1) Ankle fracture	
	2) Chest contusion (discus)	
2	Cross Country	
	(Female)	
	Stress fracture — tibia	1
	(Male)	
	Stress fracture — tibia	1
1	Hockey	
	Wrist fracture	
1	Field Hockey	
	Ankle fracture	
1	Softball	
	Metatarsal fracture	

Table VII

	Severe	Stress fracture
Male	31	1
Female	9	3

Table VIII. Football Injuries By Position

Offense	77	Defense	36
Runningbacks	36	Defensive backs	5
Quarterbacks	9	Linebackers	7
Receivers	16	Linemen	24
Linemen	15		
Kickers	1		
	77		36

Summary

Supported by a grant from the Rhode Island Foundation, a study of school athletic injuries was completed for the 1985-86 school year. Data were gathered according to sport, type, location, severity, and position. It is our goal that based on these data an improved understanding of the mechanism of injury and associated factors will lead to modifications that will improve injury prevention in these young athletes.

per cent of all soccer injuries, whereas the Indianapolis experience reported was 9.7 per cent.[3] The fracture rate in Rhode Island will be studied further to determine if improved conditioning or other preventative measures are necessary.

Contact injuries accounted for 72.3 per cent of the injuries. Of interest is the number of contact injuries in so called non contact sports: soccer, basketball and even track and field. A young lady was severely injured by a discus from an adjoining field. Although only approximately 20.0 per cent of a sport is spent in actual game time, this is when 54.6 per cent of the injuries occurred.

References

[1] Blyth CS, Mueller FO: Football Injury Survey: "When and Where Players Get Hurt." Phys. Sportsmed. 2:45-51, Sept. 1974.

[2] Olson OC: The Spokane Study: High School Football Injuries. Phys. Sportsmed. 7:75-82, Oct. 1979.

[3] McCarroll JR: Profile of Youth Soccer Injuries. Phys. Sportsmed. 12:113-117, Feb. 1984.

[4] Grana WA: Summary of 1978-79 Injury Registry for Oklahoma Secondary Schools. U. Oklahoma State Med. Assoc. 72:369-372, October 1979.

[5] Reilly MF: Nature and Causes of Hockey Injuries. Athletic Training 17:88-90, Summer 1982.

[6] Snook GA: Injuries in Intercollegiate Wrestling, A.M.J. Sports Med., 10:142-144, 1982.

The Trustees of the Fiske Fund of the Rhode Island Medical Society are pleased to announce the

FISKE PRIZE FOR 1987

to be awarded for an original contribution on

"AIDS Pandemic . . . Etiology, Incidence, Distribution, & Control"

The award is named after Caleb Fiske (1753-1834), who was a Rhode Island physician and judge, Army surgeon, and a descendent of Roger Williams. Since the prize was initiated in 1836, 87 awards have been made for original contributions. Previous recipients include Charles V. Chapin, Providence, internationally known for his research on public health; David King, Jr., Newport who received the award in 1836 for his paper on "Purpura Haemorrhagica: Its Causes and Treatment"; and Alton Oschner, New Orleans, who received the 1958 award for his paper entitled "Bronchogenic Carcinoma: Predisposing Causes."

The award for the 1987 Fiske Prize will be a maximum of $2,500. The Trustees reserve the right to award one or more prizes. The competition is not restricted to physicians.

Guidelines:

1) The original and one copy must be submitted by Aug. 24, 1987 to Secretary, Caleb Fiske Fund of the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903.
2) All papers must be double-spaced and should not exceed 10,000 words.
3) The award recipient must transfer copyright privileges to the Trustees of the Caleb Fiske Fund of the Rhode Island Medical Society. The paper will be considered for publication in the *Rhode Island Medical Journal*, subject to review by the Editorial Board.
4) The award recipient will also present his/her prize winning paper at a symposium to be scheduled in the Fall commemorating the 175th anniversary of the Rhode Island Medical Society.

PERIPATETICS

David B. Stoll, chief of hematology oncology at The Woonsocket Hospital, was recently elected vice president of medical affairs of the American Cancer Society, Northeastern Division. He was also elected a member of the New England Cancer Society.

• • •

The Rhode Island Services for the Blind and Visually Impaired recently awarded its Distinguished Service Award to **Robert S. L. Kinder,** Chief of Ophthalmology at Rhode Island Hospital. During the last sixteen years, he has annually donated one month of his time to St. Jude's Hospital in the West Indies, providing free surgery to those in need of treatment.

• • •

Naeem M. Siddiqi was recently elected to the board of directors of the northern unit of the American Cancer Society. He was also elected to membership of the New England section of the American Urological Association. He is in the Department of Urology at Pawtucket Memorial Hospital.

• • •

At the recent annual meeting of the Rhode Island affiliate, American Diabetes Association, **Stephen J. Richman** was elected president. An ophthalmologist, he specializes in cataract, glaucoma, and laser surgery.

• • •

Paul Calabresi, chairman of the Department of Medicine, vice president for academic affairs, and physician-in-chief at Roger Williams General Hospital, Providence, RI, and **Milton W. Hamolsky,** professor of medical science at Brown University and secretary of the Rhode Island Medical Society, were among 13 leading medical educators and investigators honored with mastership at the recent 68th annual scientific meeting of the American College of Physicians (ACP) held in New Orleans, LA. The awards are given for personal character, eminence in medical research, achievements in medicine or science, and service to the College. Calabresi was honored for his research contributions in clinical pharmacology of antineoplastic agents and Hamolsky for his research on the thyroid.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

R.I. Marriage and Family Therapy Center

INDIVIDUAL,COUPLE & FAMILY COUNSELING
CONFIDENTIAL-PROFESSIONAL
SLIDING FEE SCALE
CONSULTATIONS AVAILABLE

EVENINGS BY APPOINTMENT

84 LYMAN AVENUE
WARWICK, RHODE ISLAND
02888

(401)467-6290

Bruce A. Gunther, M.S.
Trained Marriage & Family Therapist

ZOVIRAX®
(acyclovir)
CAPSULES

Prevent genital herpes recurrences month after month with daily therapy.

(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

Please see last page of this advertisement for brief summary of prescribing information.

ZOVIRAX® (acyclovir) CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes, as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next page.

Prevent recurrences month after month*

ZOVIRAX®
(acyclovir)
CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psychosocial difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies,. the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance $\leq$10 ml/min/1.73/m^2.

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200"- Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

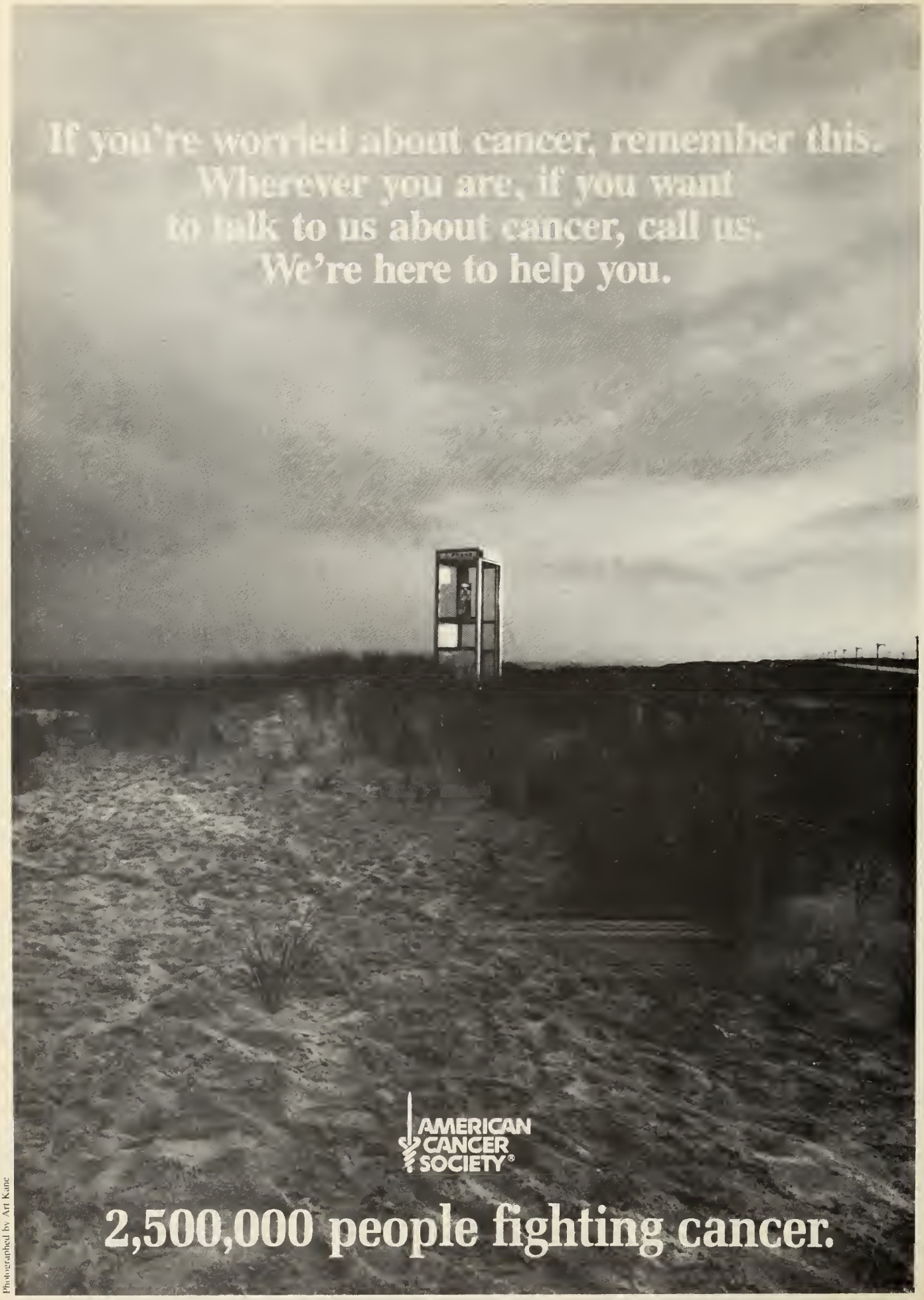
Store at 15°-30°C (59°-86°F) and protect from light.

---

*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

Wellcome | **Burroughs Wellcome Co.**
Research Triangle Park
North Carolina 27709

Copr. © 1986 Burroughs Wellcome Co. All rights reserved. 86-ZOV-5



Photographed by Art Kane

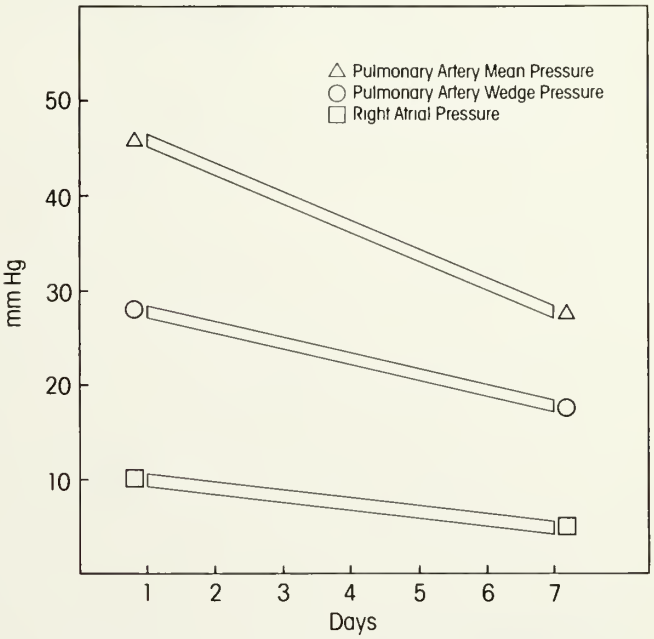
Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml
and 10-ml vials (0.25 mg/ml)

REDUCES FLUID OVERLOAD and eases the burden on the failing heart

Significantly improves hemodynamics



Ten patients with CHF showed marked hemodynamic improvement after seven days of BUMEX® (bumetanide/Roche) (mean values ± SE) Adopted from Olesen, *et al* [1]

References: **1.** Olesen KH, *et al Postgrad Med J 51* (Suppl 6) 54-63, 1975 **2.** Handler B, Dhingra RC, Rosen KM *J Clin Pharmacol 21* 706-711, Nov-Dec 1981 **3.** Brater DC, *et al Clin Pharmacol Ther 34* 207-213, Aug 1983 **4.** Brater DC, Fox WR, Chennavasin P *J Clin Pharmacol 21* 599-603, Nov-Dec 1981 **5.** Davies DL, *et al Clin Pharmacol Ther 15* 141-155, Feb 1974

BUMEX®
bumetanide/Roche
0.5-mg, 1-mg and 2-mg scored tablets,
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)

BUMEX® (bumetanide/Roche)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome
Almost equal diuretic response occurs after oral and parenteral administration of Bumex If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity
CONTRAINDICATIONS: Anuria Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment
WARNINGS: Dose should be adjusted to patient's needs Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risks to the patients
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved The potential for ototoxicity increases with intravenous therapy, especially at high doses
Patients allergic to sulfonamides may show hypersensitivity to Bumex
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets Hyperuricemia may occur Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency Bumex may increase urinary calcium excretion.
Possibility of effect on glucose metabolism exists Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions.
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously
Since lithium reduces renal clearance and adds a high risk of lithium toxicity it should not be given with diuretics
Probenecid should not be administered concurrently with Bumex
Concurrent therapy with indomethacin not recommended
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage
Interaction studies in humans have shown no effect on digoxin blood levels
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity
Pregnancy Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus
Bumetanide may be excreted in breast milk
Pediatric Use Safety and effectiveness below age 18 not established
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease)
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium. Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGDT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts Increases in urinary glucose and urinary protein have also been seen
DOSAGE AND ADMINISTRATION:
Oral Administration The usual total daily dosage is 0 5 to 2 0 mg and in most patients is given as a single dose
Parenteral Administration Administer to patients (IV or IM) with GI absorption problem or who cannot take oral The usual initial dose is 0 5 to 1 mg given over 1 to 2 minutes If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day
HOW SUPPLIED: *Tablets*, 0 5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescription Paks of 30, Tel-E-Dose® cartons of 100 Imprint on tablets 0 5 mg—ROCHE BUMEX 0.5, 1 mg—ROCHE BUMEX 1, 2 mg—ROCHE BUMEX 2
Ampuls, 2 ml, 0 25 mg/ml, boxes of ten
Vials, 2 ml, 4 ml and 10 ml, 0 25 mg/ml, boxes of ten

ROCHE®
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc
Nutley, New Jersey 07110

ROCHE

OVERLOAD

Reduce fluid volume and improve hemodynamics in CHF

Edema due to congestive heart failure often demands highly effective diuresis to reduce the fluid load on the failing heart. Bumex® (bumetanide/Roche) is the next generation in loop diuretic therapy for three powerful reasons. It moves out an unsurpassed volume of fluid and sodium, resulting in significant reductions in edema and right atrial and pulmonary artery wedge pressures.[1,2] It's almost completely absorbed through the GI tract, so it's easy to titrate.[3] And Bumex completes high-volume diuresis fast—within four hours at usual doses.[4,5] Your patients spend less time in diuresis, more time in normal activities.

Bumex has a good safety profile; however, as with all loop diuretics, Bumex, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion, including hypokalemia. Serum electrolytes should be monitored periodically, especially in patients on low salt diets or those treated for prolonged periods or on high doses.

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

Bumex® BUMEX 2
bumetanide/Roch

0.5-mg, 1-mg and 2-mg scored tablets, 2-ml ampuls (0.25 mg/ml) and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

First line loop diuretic therapy

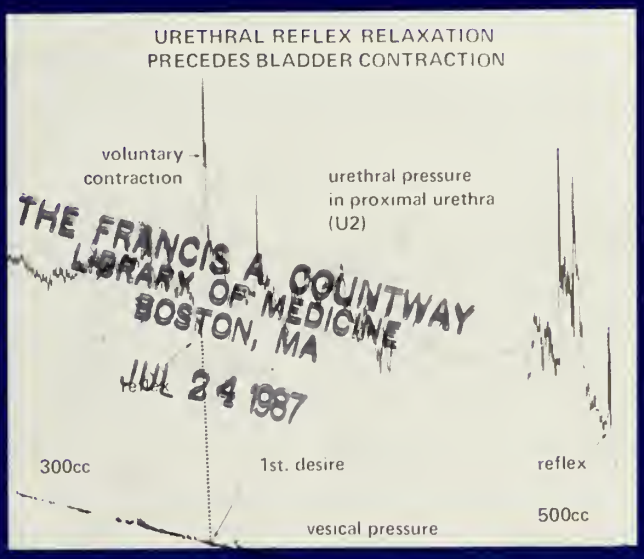
Please see references and summary of product information on preceding page.

Copyright © 1986 by Hoffmann-La Roche Inc. All rights reserved

Rhode Island Medical Journal

July 1987
Volume 70, Number 7

DISPLAY SHELVES



THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
JUL 24 1987

FEMALE UROLOGY

CONTRIBUTIONS

293 The Challenge of Assessing and Treating Female Incontinence

307 Single Dose Therapy of Acute Urinary Tract Infection in Women Using Trimethoprim — Sulfamethoxazole: Experience in a Prepaid Internal Medicine Group Practice

311 Rhode Island Physicians' Recognition and Reporting of Adverse Drug Reactions

319 Children and the Space Shuttle Tragedy

287 EDITORIAL

289 EDITOR'S MAILBOX

317 CONTINUING MEDICAL EDUCATION CALENDAR

321 HAVE YOU HEARD?

When you have substantial assets, with an income to match, your Hospital Trust Private Banker can help further your financial well-being. Call the movers and shakers of Private Banking.

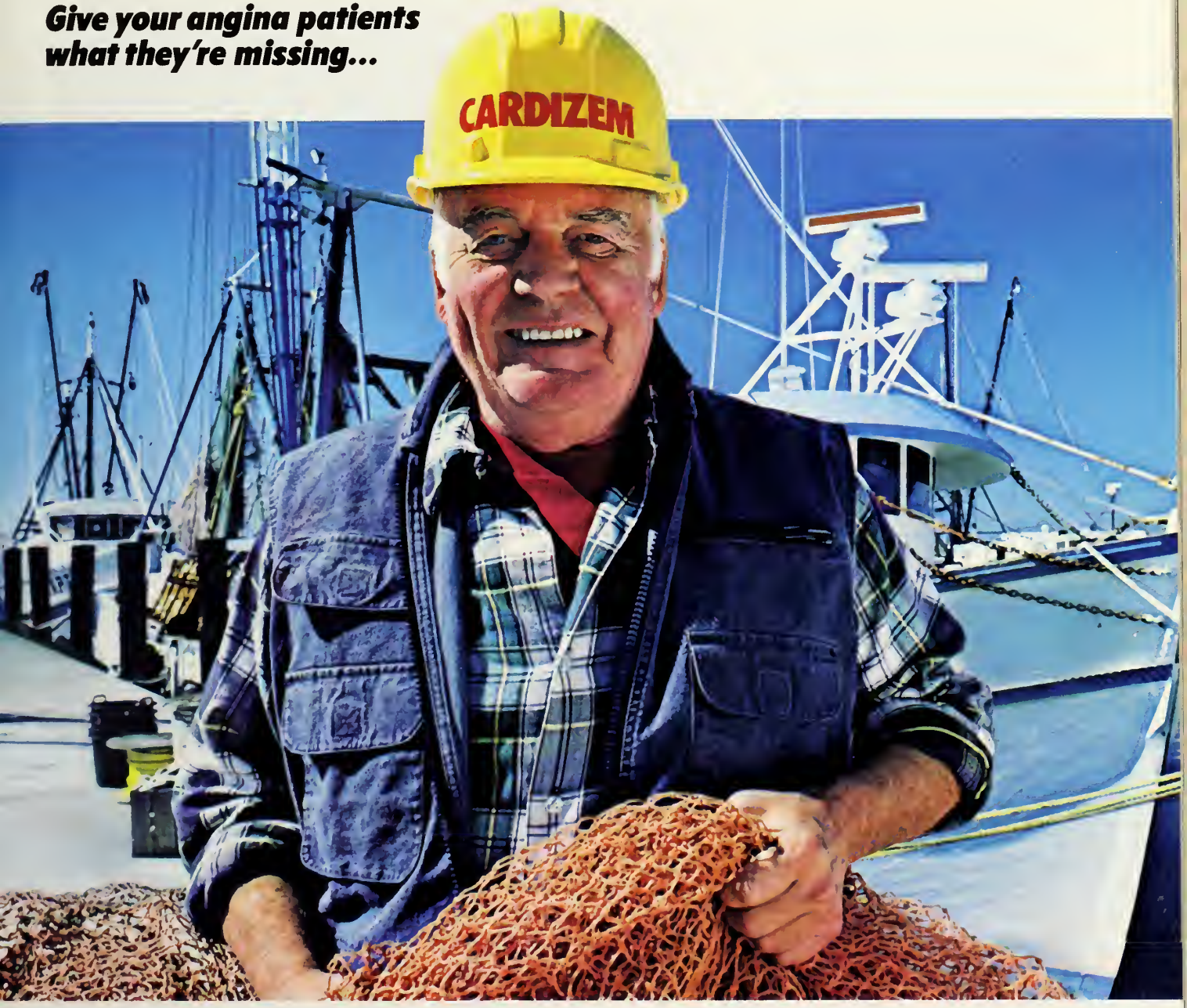
Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK
Hospital Trust
a BANK OF BOSTON company

Member FDIC

Equal Opportunity Lender

Give your angina patients what they're missing...



CARDIZEM®: FEW SIDE EFFECTS

diltiazem HCl/Marion

- ***Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate***
- ***Proven efficacy when used alone in angina[1]***
- ***Compatible with other antianginals[2,3]****
- ***A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD[4,5]***

90 mg NEW 120 mg GREATER DOSAGE FLEXIBILITY

***See Warnings and Precautions.**

Please see brief summary of prescribing information on the next page.

CARDIZEM® diltiazem HCl/Marion

FEW SIDE EFFECTS IN ANTIANGINAL THERAPY

60 mg tid or qid

Brief Summary
Professional Use Information

CARDIZEM®
(diltiazem HCl) 30 mg and 60 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).*
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS

General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.*

Drug Interaction. *Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)*

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses at 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope*
Nervous System:	*Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria.*
Other:	*Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

Issued 7/86

See complete Professional Use Information before prescribing.

References: ***1.*** *Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983, 106(6):1341-1347.* ***2.*** *Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984,24(Dec):150-159.* ***3.*** *Johnston DL, Lesowoy R, Humen DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985,55:680-687.* ***4.*** *Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39.* ***5.*** *Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982,50(Sept):94-116.*

Another patient benefit product from

PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC.
KANSAS CITY, MO 64137

0246M6

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL® LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were treated merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

NOW AVAILABLE...
NEW LOW DOSE
INDERAL LA 60 mg
LONG ACTING CAPSULES
(PROPRANOLOL HCl)

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION "SEE PACKAGE CIRCULAR")*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. INDERAL LA is formulated to provide a sustained release of propranolol hydrochloride. INDERAL LA is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (60, 80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period, the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL Tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours, then decline exponentially.

INDERAL LA should not be considered a simple mg-for-mg substitute for conventional propranolol, and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered, especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension. It may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first-degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (eg, chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta blockers should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. Following insulin-induced hypoglycemia, propranolol may cause a delay in the recovery of blood glucose to normal levels.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol may change thyroid function tests, increasing T_4 and reverse T_3, and decreasing T_3.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. GENERAL. Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

CLINICAL LABORATORY TESTS. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Caution should be exercised when patients receiving a beta blocker are administered a calcium-channel-blocking drug, especially intravenous verapamil, for both agents may depress myocardial contractility or atrioventricular conduction. On rare occasions, the concomitant intravenous use of a beta blocker and verapamil has resulted in serious adverse reactions, especially in patients with severe cardiomyopathy, congestive heart failure or recent myocardial infarction.

Aluminum hydroxide gel greatly reduces intestinal absorption of propranolol.

Ethanol slows the rate of absorption of propranolol.

Phenytoin, phenobarbitone, and *rifampin* accelerate propranolol clearance.

Chlorpromazine, when used concomitantly with propranolol, results in increased plasma levels of both drugs.

Antipyrine and *lidocaine* have reduced clearance when used concomitantly with propranolol.

Thyroxine may result in a lower than expected T_3 concentration when used concomitantly with propranolol.

Cimetidine decreases the hepatic metabolism of propranolol, delaying elimination and increasing blood levels.

Theophylline clearance is reduced when used concomitantly with propranolol.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

PREGNANCY. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose. There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS. INDERAL is excreted in human milk. Caution should be exercised when INDERAL (propranolol HCl) is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. Bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. Light-headedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, vivid dreams, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics. For immediate formulations, fatigue, lethargy, and vivid dreams appear dose related.

Gastrointestinal. Nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. Pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. Bronchospasm.

Hematologic. Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. Alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL Tablets to INDERAL LA Capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg-for-mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION—*Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS—*Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three- to seven-day intervals until optimal response is obtained. Although individual patients may respond at any dosage level, the average optimal dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE—*Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimal migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximal dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS—80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE—At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol and metoprolol given once daily. *Arch Intern Med* 1985; 145:1321-1323.

R 7119 587

Ayerst AYERST LABORATORIES
New York, NY 10017

© 1987 Ayerst Laboratories

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
JUL 24 1987

July 1987
Volume 70, Number 7

Rhode Island Medical Journal

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Member of Publications Committee

***Edward R. Feller, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***Guy A. Settipane, MD**

***David T. Barrall, MD**
Resident

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401 331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

RHODE ISLAND AIR NATIONAL GUARD

PART TIME

MEDICAL OFFICER POSITIONS AVAILABLE

OPEN TO:
MEDICAL AND/OR
OSTEOPATHIC DOCTORS

CONTINUING MEDICAL EDUCATION

FOR MORE INFORMATION CONTACT:
COL (DR) BLAS MORENO
(401) 726-2555

"BEST PART-TIME JOB IN AMERICA"

TABLE OF CONTENTS

287 **EDITORIAL**

Long-Term-Care Insurance

Seebert J. Goldowsky, MD

289 **EDITOR'S MAILBOX**

317 **CONTINUING MEDICAL EDUCATION CALENDAR**

321 **HAVE YOU HEARD?**

CONTRIBUTIONS

293 **The Challenge of Assessing and Treating Female Incontinence**

A Complete Urodynamic Evaluation Should Precede Intervention

Jacques G. Susset, MD

307 **Single Dose Therapy of Acute Urinary Tract Infection in Women Using Trimethoprim — Sulfamethoxazole: Experience in a Prepaid Internal Medicine Group Practice**

Single Dose Therapy in Women is Safe, Effective, and Well Tolerated

Stephen F. Quevedo, MD
Barbara Chace, NP
Susan Kaemmerlen, NP

311 **Rhode Island Physicians' Recognition and Reporting of Adverse Drug Reactions**

Increased Physician Participation in Post-Marketing Surveillance Will Lead to Greater Understanding of Adverse Drug Reactions

H. Denman Scott, MD, MPH
Sara E. Rosenbaum, PhD
William J. Waters, PhD
Avery M. Colt, MA
Lisa G. Andrews, MBA
John P. Juergens, PhD
Gerald A. Faich, MD, MPH

319 **Children and the Space Shuttle Tragedy**

A Strategy Should be Developed for Dealing with Traumatic National Events

Shawn Cooper, PhD, MPH

COVER: *Photograph from Dr. Susset's article, "The Challenge of Assessing and Treating Female Incontinence." See page 293.*

AIM HIGH

DOES YOUR PRACTICE NEED A NEW PERSPECTIVE

LOOK INTO AIR FORCE AEROSPACE MEDICINE.

As an Air Force Flight Surgeon you will have a truly general practice in your office. In the air you'll fly with and observe air crew members—adding a new perspective to your medical career.

You can be an Air Force Flight Surgeon. Leave the headaches of office overhead paperwork. Enjoy 30 days of vacation with pay each year, time for your family, medical and dental care, low cost life insurance plus a generous noncontributory retirement program. Maybe it's about time to give your life a new perspective.

Contact your nearest Air Force recruiter and examine your opportunities in aerospace medicine today! Call

SSgt A. J. Avila
(401)528-4044
Collect

AIR FORCE

EDITORIAL

Long-Term-Care Insurance

Soon after the announcement of a catastrophic health care plan for the elderly as the "last full measure of security" by the Reagan administration, we pointed out in these columns that it was a snare and a delusion and that long-term-care coverage was the real and pressing need of the aging. Under present law they must pauperize themselves before they are eligible for federal assistance. At the time of our previous editorial comment there were a few rumblings in the insurance industry suggesting a realization of this need. Since then the media and politicians have increasingly turned their attention to the problem. A few quotations may be in order:

- "What has been presented as catastrophic health care insurance is a hoax." — US Rep Henry Waxman, (D-Calif).
- "Simply put, [the President's] plan would help only three per cent of the total Medicare population." "What a tragedy it would be to accept a pygmy step forward instead of what has been described as a giant step." — US Rep Claude Pepper (D-Fla).
- "We are willing to patch holes in the 'umbrella' of catastrophic care one piece at a time." "Acute care is the little patch that the President and Congress have picked first, but they may be starting with the wrong patch." — Executive Director Cyril F. Brickfield, American Association of Retired People (AARP).

A survey of its members by the Health Insurance Association of America (HIAA) found that as of January 1, 1986, 13 companies offered long-term-care insurance with a combined subscription base of 130,000. Since then, at least four more of the 335 commercial insurers in HIAA have entered the market, and another 20 have announced plans to introduce a policy, with policy holders currently numbering 200,000 or more. According to Stanley Wallack, director of the Health Policy Center at Brandeis University, "We're no longer as overwhelmed by what we see as the potentially huge burden of costs." Long-term care, he pointed out, is the major catastrophic health care expense for the elderly. With the increasing numbers of people in their 40s and 50s with parents in their 60s and 70s, they are more and more confronted with the problem. "I don't think there's any question," he added, "that the interest level out there is going to increase." With the federal government skittish about facing up to the cost, there is a general move to encourage the private market.

In a marketing survey by Blue Cross and Blue Shield more than half of those interviewed said they would be interested in a plan if offered. More than 30 per cent of 200 large corporations questioned indicated that they were interested in making coverage available to their employees. Blue Cross and Blue Shield of Washington and Alaska has sold 1000 policies in a pilot program. Eight other Blues plans are scheduled to introduce such insurance in 1987.

On May 1, 1987 Aetna Life Insurance Co. offered 7500 state of Alaska retirees and their spouses the country's first employer-based long-term-care insurance plan. This plan will cover "the usual, reasonable, and customary" costs up to a maximum. Aetna has in prospect employer-based plans including Ohio state retirees, Kentucky school teachers, American Express, Hallmark, and Aetna's own employees. Metropolitan Life Insurance Co. announced recently that it would offer long-term-care benefits to enrollees in the Group Health Cooperative of Puget Sound, based on Health Maintenance Organization (HMO) membership rather than employment.

Constance Horner, director of the US Office of Personnel Management in the Reagan administration, has proposed offering the federal workers a long-term-care coverage option to the traditional life insurance coverage available to government employees. It allows for conversion of all or part of the life insurance up to $25,000 to nursing home or home health care payments at $40 and $20 per day respectively, which, of course, is not full coverage.

In the meantime Rep Claude Pepper has proposed a federal plan that would add $50 per month to the Part B premium. In no case, however, would the cost of health premiums exceed $800 a year or 10 per cent of income. Those earning more than $44,000 per year would be required to pay 1.45 per cent on all wage and

salary income. Nevertheless, because of budget restraints it is unlikely that any bill going beyond the administration's proposed catastrophic coverage is likely to pass. The federal government has set aside a special ten-foot pole for not touching nursing home care. It isn't the principle of the thing, it's the money.

As Wallack of Brandeis has stated, "Now that we know a government solution is not iminent, we realize we are going to have to sell products in the market, and we're going to have to find products that are attractive to the elderly." It appears that, however haltingly, the process has begun.

Seebert J. Goldowsky, MD

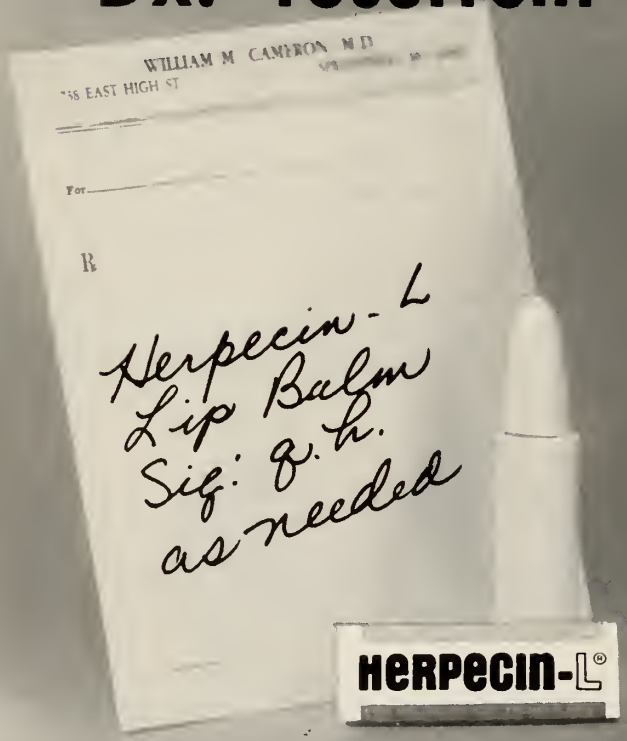
ERRATA

RIMJ 69:507-508, November 1986

EDITORIAL: A Tribute to Seebert J. Goldowsky

Page 507, paragraph two, first column, line four, omit the words "also summa cum laude." Paragraph two, first column, line six, "Beth El Hospital in Boston" should read "Beth Israel Hospital in Boston." Paragraph two, first column, line 17, "European Theater of Operations," should read "Southwest Pacific Area." Page 508, paragraph one, first column, line ten, "Peter P. Chace" should read "Peter Pineo Chase." Paragraph one, first column, line 14, "Dr. John Donnelly" should read "Dr. John Donley."

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

EDITOR'S MAILBOX

United Way Thank-You

To The Editor:

"Consider yourself hugged by the half million Rhode Islanders your United Way gift helps."

To me, this year's United Way slogan seems particularly appropriate in regard to Rhode Island physicians. As I conclude my second year of involvement with the United Way, I want to express my deep appreciation to the physicians of Rhode Island for their outstanding support.

While serving as Chair of the United Way Leadership Committee, I have noted with increasing pleasure the growing commitment of physicians to the community they serve through the United Way.

The figures show that your concern is unprecedented. Thanks to your generous participation, Rhode Island physicians' contributions have risen by 66 per cent in the last two years and have increased in participation by an impressive 25 per cent over the last year.

Numbers and statistics are gratifying indeed. However, they are most meaningful as they reflect that Rhode Island physicians are concerned that urgent community needs be met — day care for working parents, hope for the depressed and suicidal, guidance for teenage parents, help for battered women and children, and much more. Your contributions have ensured that such help will be available when it is needed.

On behalf of the agencies, the United Way and my fellow physicians on the Physicians' Leadership Committee — thank you.

Dugald H. Munro, Chairman
United Way Physicians' Leadership Committee

Follow-up on National Cancer Institute (NCI) Funded Project:

To The Editor:

Three years ago in this *Journal* we described a new National Cancer Institute (NCI) funded project, "A Study of Treatment Choices Affecting Elderly Cancer Patients," that was about to begin in Rhode Island. The purpose of this letter is to update physicians and other health care personnel throughout the state regarding the status of this project and to thank all who have cooperated with this effort during the last three years.

The project involves an evaluation of issues related to cancer diagnosis and management in the elderly. This is a cooperative effort which seeks to integrate the knowledge and resources of patients, physicians, and hospitals throughout the state. The population being studied is all Rhode Island residents between the ages of 45 and 90 with newly diagnosed lung, breast, and colorectal cancer. Through medical records, we document diagnostic procedures as well as the surgical, chemotherapeutic, and radiation interventions received by patients. This information is collected over the twelve-month period following each patient's diagnosis. Treatment and outcome data are provided through physician and patient interview. We have requested from physicians the initial treatment recommendation(s) made for each patient. With physician and patient permission, patients were interviewed at three points over the twelve month follow-up period.

Patients were identified between July 1984 and February 1986 through pathology offices at Rhode Island, Roger Williams General, Kent County Memorial, Pawtucket Memorial, Miriam, St. Joseph, and Woman and Infants Hospitals, and at the Veterans Administration Medical Center. Eligibility was confirmed through review of

patients' medical records by trained abstractors. A total of 1,581 patients were identified as study eligible. This number is expected to represent between 70 per cent to 80 per cent of all such patients diagnosed in the state during this time.

We have been very pleased with the degree of physician cooperation received. A total of 460 physicians have been contacted by us at one time or another. Only 11 physicians have refused to be involved in any aspect of the study. Nearly three-quarters (74 per cent) of all treatment recommendation forms sent to physicians were returned. Permission was granted for patient interviews in 81 per cent of the cases in which it was requested. Analysis has shown that physicians were less likely to permit contact with patients who were older, less functional, or both patients. Cooperation has also been outstanding from physicians when they are approached regarding access to their office medical records. In addition to hospital data collection, medical data is being abstracted in the private offices of 15 medical and radiation oncologists.

Patient cooperation has been excellent. Only 20 per cent of patients contacted refused to take part in our initial interview. A total of 707 patients were interviewed initially, 595 patients were re-interviewed three months later, and 490 patients have been interviewed twelve months after diagnosis. Drop-out rates have been low following the initial interview, with attrition due to death as the primary cause of no follow-up interview.

Final data analyses have begun. By August of this year we hope to complete investigations of our major research questions. These deal with the relationship between age and: hesitation in seeking medical care, extent of disease at diagnosis, and physician treatment recommendations at diagnosis. Using data collected over the twelve-month follow-up period, we will relate the characteristics of treatments received by patients, their functional status, and their quality of life to age.

Within the next several months we shall begin a new project which will extend the study of this population into the areas of health care costs and patient financial burden. Hospital review boards and physicians will be contacted to explain this extension more fully.

Finally, we should again like to thank all who have cooperated with us in carrying out this project. Without your assistance this type of systematic research on elderly patients would not be possible. In speaking with our epidemiologist colleagues across the country, they are astonished at the comprehensiveness of the project and at the degree of cooperation we have received. This is only possible due to the cooperation of the Rhode Island medical community. Any further information about this project may be obtained by contacting the Center for Health Care Research at Brown University (863-3490).

Vincent Mor, PhD, Principal Investigator
Edward Guadagnoli, PhD
Frank J. Cummings, MD
Arvin Glicksman, MD
Richard Goldberg, MD
Rebecca Silliman, MD
Marsha Fretwell, MD
Centers for Long Term Care Gerontology and Health Care Research
Brown University
Box G
Providence, RI 02912

More On HMOs

To The Editor:

In the February issue of the *Rhode Island Medical Journal,* you published an article by a physician "in the trenches" who is writing about his personal experiences with an HMO.

This is followed by a commentary from the medical director of a local HMO. Two points are quickly obvious: the two HMOs under discussion are very different in concept and design. The medical director does not like what he reads and dismisses first-hand experiences from his evaluation.

What is needed is an article on the real disease process here — it is called capitation. It is a business concept that destroys the social contract between doctor and patient, which is the heart of medicine as practiced in this country, and the basis for responsible conduct. I believe an entire issue should be devoted to capitation, educating physicians as to its history, physical findings, diagnosis, and treatment.

Robert D. Corwin, MD
111 Plain Street
Providence, RI 02903

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:

- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

Table 1. Physio-Pathological Classification of Female Urinary Incontinence.

Urethral Factors

1. Transvaginal displacement of the urethra
2. Degree of vesical neck resistance
3. Quality of the voluntary sphincteric contraction
4. Compliance of the urethral wall
5. Length of the urethra
6. Urethral relaxation reflex

Vesical Factors

Vesical hyperactivity secondary to:
- — Obstruction
- — Inflammation
- — Neurologic lesion
- — Vesical neck patency

Primary:
- — Idiopathic

Vesical Capacity
- — Large or contracted bladder

Polyuria
Psychogenic factors

A *Vesical Factors*

1 *Detrusor Hyperreflexia* (Fig 1). The most common bladder anomaly causing incontinence is detrusor hyperreflexia. It is also called bladder instability, although hyperreflexia is a better term. It is literally bladder contraction without the permission of its owner.

Etiology. a) *Neurogenic.* Hyperreflexia is by definition a neurogenic phenomenon whether or not the lesion can be demonstrated. In some instances, the presence of an upper motor neuron lesion is obvious. Any complete or incomplete spinal cord destruction or compression affecting the motor pathways may initially cause detrusor hyperreflexia. The associated, objective neurological findings make the diagnosis easy. Similarly, a cerebrovascular accident followed by hemiplegia offers no diagnostic difficulty.

The diagnosis is also easy when a demyelinating disease is obvious or when other neurological symptoms indicate the presence of an upper motor neuron lesion. On the other hand, we have recently observed[2] six cases of intervertebral disks and spondylosis affecting one or several levels of the spinal cord causing urinary dysfunction and particularly detrusor hyperreflexia without evidence of other neurological deficit.

b) *Obstructive.* Outlet obstruction is another cause of detrusor hyperreflexia. A hypertrophic, trabeculated detrusor is hyperactive. The bladder cannot tolerate overfilling in the presence of the obstruction since too high a volume would mean a thinner wall and consequently less power per cm.[2] The receptor threshold is lowered and an alarm system is set up which is reflected in the increased sensation of urgency and frequent voiding. Objectively, such a situation results in the early appearance of spontaneous non-inhibited contractions on cystometrogram.

The relief of obstruction usually results in the disappearance of hyperreflexia unless an associated neurological lesion is present. Detrusor hyperreflexia appears to be very common in the older population even when objective neurological findings are absent. This is likely due to minimal localized cortical or subcortical ischemia affecting the inhibitory pathway. It would explain the persistence of detrusor hyperreflexia following a prostatectomy for instance. This possibility justifies performing a cystometrogram routinely as part of the workup before surgery for obstruction.

There is a significant difference in the types of detrusor hyperreflexia observed in cases of obstruction and upper motor neuron lesion. With A. Brissot, we recently reviewed data on 51 patients; 31 had proven upper motor neuron lesions, while 20 presented with outlet obstruction. The degree of reflexivity expressed by the volume at which uninhibited contractions occurred

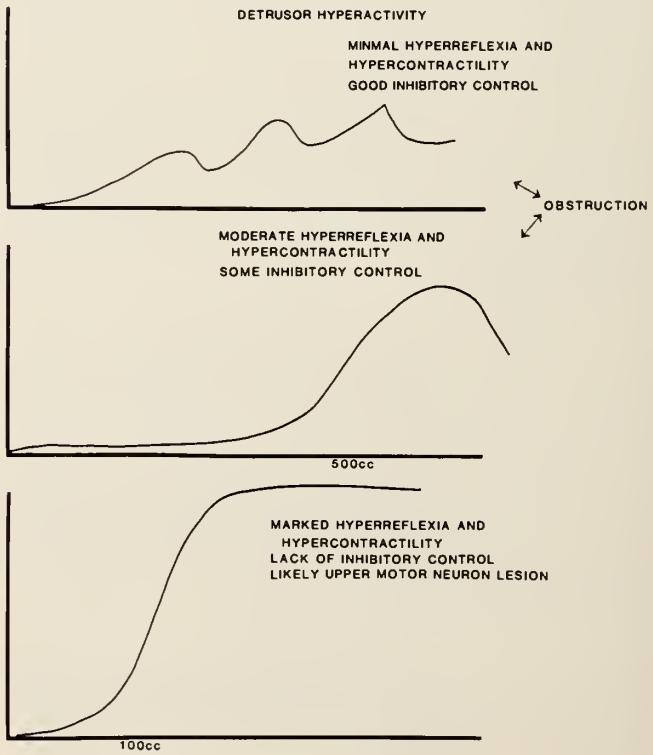


Fig 1. Detrusor Hyperreflexia.

was 207 ± 123ml in the neurological group and 490 ± 193ml in the obstructive group (Fig 2). This difference was highly significant (p .001). There was a good correlation (r = .61) between reflexivity and amplitude of the contraction in the neurological group and a poor correlation between these two parameters (r = .10) in the obstructive group. It means that even in the presence of obstruction a strong contraction occurring at low volume and in the supine position argues in favor of an upper motor neuron lesion and calls for further investigation. According to Siroky[3] a lesion below the pons causes bladder spasm of lower amplitude than a lesion above it. The pons act as an amplifier of the bladder contraction.

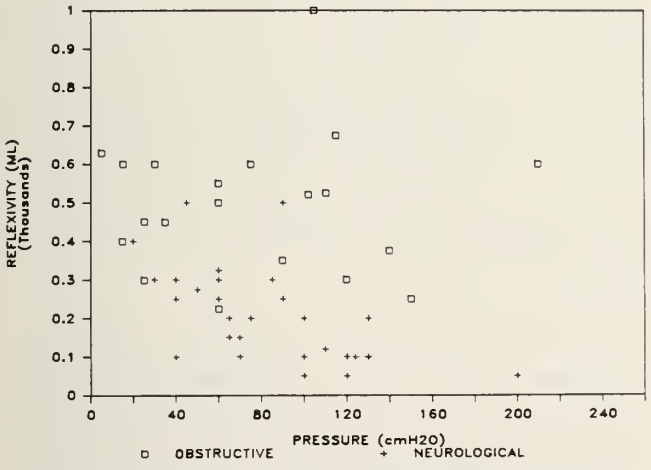


Fig 2. In case of upper motor neuron lesion uninhibited detrusor contraction occurs earlier and is of higher amplitude than in case of obstruction.

c) *Local Inflammation.* Urethral and vesical inflammation constitutes another cause for detrusor hyperreflexia. Urgency is part of the picture of urethritis and cystitis. Although cystometric findings in cases of inflammation are poorly documented, they appear to follow closely the presence or absence of urgency. Arnold stated that females presenting neither frequency nor urgency had only a 5 per cent chance of having objective evidence of hyperreflexia on cystometrogram. On the contrary, if urgency and frequency are present, the incidence of objective hyperreflexia is 55 per cent. Inflammation appears to lower the threshold of stretch receptors. In the case of hyperreflexia, the common demoninator is indeed the level of sensitivity of the intramural receptors. Whether it is influenced by a local factor such as obstruction or inflammation, by a central nervous system lesion, or by a subconscious disposition such as a particular conditioned reflex (ie, the sound of running water causing urgency, or the garage door syndrome). It is, therefore, artificial and of little relevance to distinguish sensory from motor urgency or urgency incontinence. What really counts is the volume at which hyperreflexia occurs in a given position. Identification, measurement, and correlation of factors influencing receptor sensitivity is a direction for future research.

d) *Vesical Neck Patency.* Another factor in detrusor hyperreflexia may be the presence of abnormal vesical neck patency. There are two arguments in favor of this possibility. We were able to demonstrate abnormal vesical neck patency in females complaining of urgency incontinence occurring exclusively in the sitting or standing position. McGuire[4] showed that urethrocystopexy could cure detrusor hyperreflexia. Since one of the mechanical effects of this operation is to reduce vesical neck patency, it is indeed likely that such abnormal patency was a primary cause of the bladder hyperreflexia. Urine leaking into the proximal urethra can stimulate a detrusor reflex contraction. The difference in the occurrence of incontinence in supine and sitting positions may be explained on this basis.

The occurrence of detrusor hyperreflexia in the etiology of female incontinence varies with the series. It may reach 62 per cent.[5] In one of our series, symptoms of detrusor hyperreflexia, that is urgency, frequency were present in 102 of 141 females presenting with incontinence, or 72 per cent. Only 28 per cent of these patients presented exclusively with stress incontinence.[6]

2 *Abnormal vesical compliance* (Fig 3). Both a small contracted bladder and at the opposite extreme a large bladder with high residual urine may contribute to the occurrence of incontinence. A bladder of 100ml capacity usually has low compliance and high pressure and will be full constantly resulting in excessive demand on an overwhelmed sphincter mechanism. A 300 to 500ml residual of urine in a highly compliant bladder on the other hand will have a tendency to exagerate vesical neck patency and promote leakage. Polyuria resulting from excess fluid intake or diabetes insipidus may have the same effect in enhancing detrusor-sphincter imbalance.

Table 1. Physio-Pathological Classification of Female Urinary Incontinence.

Urethral Factors

1. Transvaginal displacement of the urethra
2. Degree of vesical neck resistance
3. Quality of the voluntary sphincteric contraction
4. Compliance of the urethral wall
5. Length of the urethra
6. Urethral relaxation reflex

Vesical Factors

Vesical hyperactivity secondary to:
- — Obstruction
- — Inflammation
- — Neurologic lesion
- — Vesical neck patency

Primary:
- — Idiopathic

Vesical Capacity
- — Large or contracted bladder

Polyuria
Psychogenic factors

A *Vesical Factors*

1 *Detrusor Hyperreflexia* (Fig 1). The most common bladder anomaly causing incontinence is detrusor hyperreflexia. It is also called bladder instability, although hyperreflexia is a better term. It is literally bladder contraction without the permission of its owner.

Etiology. a) *Neurogenic.* Hyperreflexia is by definition a neurogenic phenomenon whether or not the lesion can be demonstrated. In some instances, the presence of an upper motor neuron lesion is obvious. Any complete or incomplete spinal cord destruction or compression affecting the motor pathways may initially cause detrusor hyperreflexia. The associated, objective neurological findings make the diagnosis easy. Similarly, a cerebrovascular accident followed by hemiplegia offers no diagnostic difficulty.

The diagnosis is also easy when a demyelinating disease is obvious or when other neurological symptoms indicate the presence of an upper motor neuron lesion. On the other hand, we have recently observed[2] six cases of intervertebral disks and spondylosis affecting one or several levels of the spinal cord causing urinary dysfunction and particularly detrusor hyperreflexia without evidence of other neurological deficit.

b) *Obstructive.* Outlet obstruction is another cause of detrusor hyperreflexia. A hypertrophic, trabeculated detrusor is hyperactive. The bladder cannot tolerate overfilling in the presence of the obstruction since too high a volume would mean a thinner wall and consequently less power per cm.[2] The receptor threshold is lowered and an alarm system is set up which is reflected in the increased sensation of urgency and frequent voiding. Objectively, such a situation results in the early appearance of spontaneous non-inhibited contractions on cystometrogram.

The relief of obstruction usually results in the disappearance of hyperreflexia unless an associated neurological lesion is present. Detrusor hyperreflexia appears to be very common in the older population even when objective neurological findings are absent. This is likely due to minimal localized cortical or subcortical ischemia affecting the inhibitory pathway. It would explain the persistence of detrusor hyperreflexia following a prostatectomy for instance. This possibility justifies performing a cystometrogram routinely as part of the workup before surgery for obstruction.

There is a significant difference in the types of detrusor hyperreflexia observed in cases of obstruction and upper motor neuron lesion. With A. Brissot, we recently reviewed data on 51 patients; 31 had proven upper motor neuron lesions, while 20 presented with outlet obstruction. The degree of reflexivity expressed by the volume at which uninhibited contractions occurred

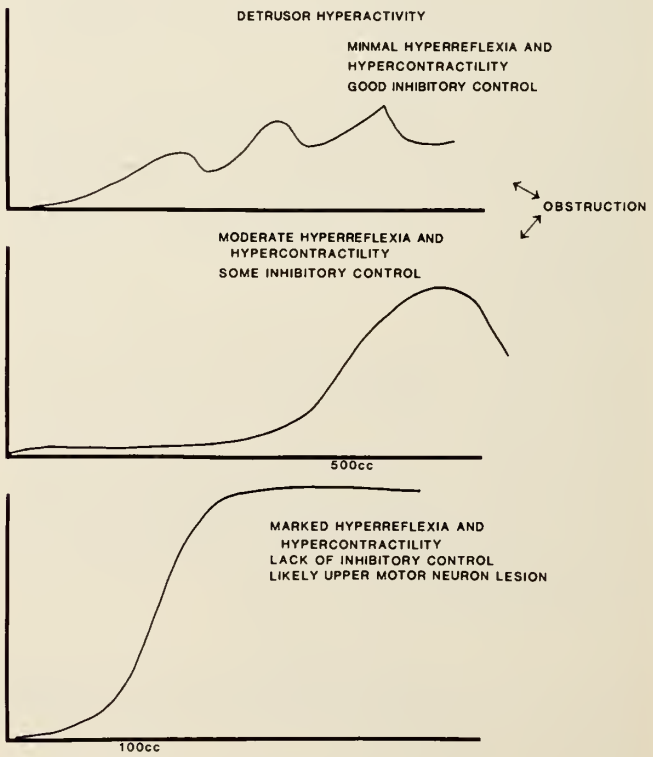


Fig 1. Detrusor Hyperreflexia.

was 207 ± 123ml in the neurological group and 490 ± 193ml in the obstructive group (Fig 2). This difference was highly significant (p .001). There was a good correlation (r = .61) between reflexivity and amplitude of the contraction in the neurological group and a poor correlation between these two parameters (r = .10) in the obstructive group. It means that even in the presence of obstruction a strong contraction occurring at low volume and in the supine position argues in favor of an upper motor neuron lesion and calls for further investigation. According to Siroky[3] a lesion below the pons causes bladder spasm of lower amplitude than a lesion above it. The pons act as an amplifier of the bladder contraction.

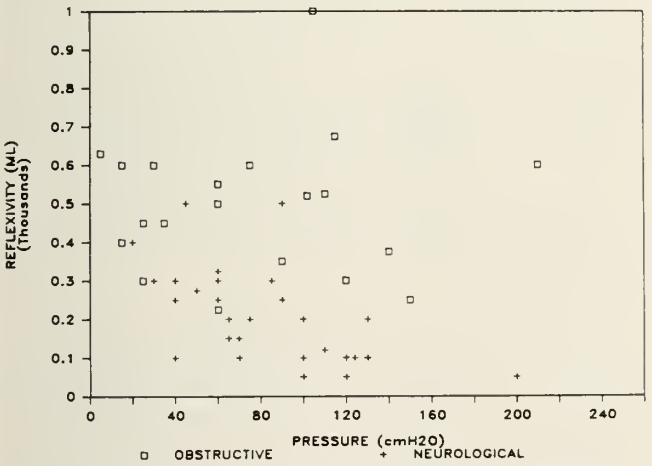


Fig 2. In case of upper motor neuron lesion uninhibited detrusor contraction occurs earlier and is of higher amplitude than in case of obstruction.

c) *Local Inflammation.* Urethral and vesical inflammation constitutes another cause for detrusor hyperreflexia. Urgency is part of the picture of urethritis and cystitis. Although cystometric findings in cases of inflammation are poorly documented, they appear to follow closely the presence or absence of urgency. Arnold stated that females presenting neither frequency nor urgency had only a 5 per cent chance of having objective evidence of hyperreflexia on cystometrogram. On the contrary, if urgency and frequency are present, the incidence of objective hyperreflexia is 55 per cent. Inflammation appears to lower the threshold of stretch receptors. In the case of hyperreflexia, the common demoninator is indeed the level of sensitivity of the intramural receptors. Whether it is influenced by a local factor such as obstruction or inflammation, by a central nervous system lesion, or by a subconscious disposition such as a particular conditioned reflex (ie, the sound of running water causing urgency, or the garage door syndrome). It is, therefore, artificial and of little relevance to distinguish sensory from motor urgency or urgency incontinence. What really counts is the volume at which hyperreflexia occurs in a given position. Identification, measurement, and correlation of factors influencing receptor sensitivity is a direction for future research.

d) *Vesical Neck Patency.* Another factor in detrusor hyperreflexia may be the presence of abnormal vesical neck patency. There are two arguments in favor of this possibility. We were able to demonstrate abnormal vesical neck patency in females complaining of urgency incontinence occurring exclusively in the sitting or standing position. McGuire[4] showed that urethrocystopexy could cure detrusor hyperreflexia. Since one of the mechanical effects of this operation is to reduce vesical neck patency, it is indeed likely that such abnormal patency was a primary cause of the bladder hyperreflexia. Urine leaking into the proximal urethra can stimulate a detrusor reflex contraction. The difference in the occurrence of incontinence in supine and sitting positions may be explained on this basis.

The occurrence of detrusor hyperreflexia in the etiology of female incontinence varies with the series. It may reach 62 per cent.[5] In one of our series, symptoms of detrusor hyperreflexia, that is urgency, frequency were present in 102 of 141 females presenting with incontinence, or 72 per cent. Only 28 per cent of these patients presented exclusively with stress incontinence.[6]

2 *Abnormal vesical compliance* (Fig 3). Both a small contracted bladder and at the opposite extreme a large bladder with high residual urine may contribute to the occurrence of incontinence. A bladder of 100ml capacity usually has low compliance and high pressure and will be full constantly resulting in excessive demand on an overwhelmed sphincter mechanism. A 300 to 500ml residual of urine in a highly compliant bladder on the other hand will have a tendency to exagerate vesical neck patency and promote leakage. Polyuria resulting from excess fluid intake or diabetes insipidus may have the same effect in enhancing detrusor-sphincter imbalance.

3 *Other factors.* Physical exercise causing marked changes in intraabdominal pressure may be a factor of incontinence when the urethral resistance is on the weak side. An effective treatment of the incontinence may well be merely reduction of the exercise, control of the condition causing the coughing (stop smoking), or a reduction of fluid intake.

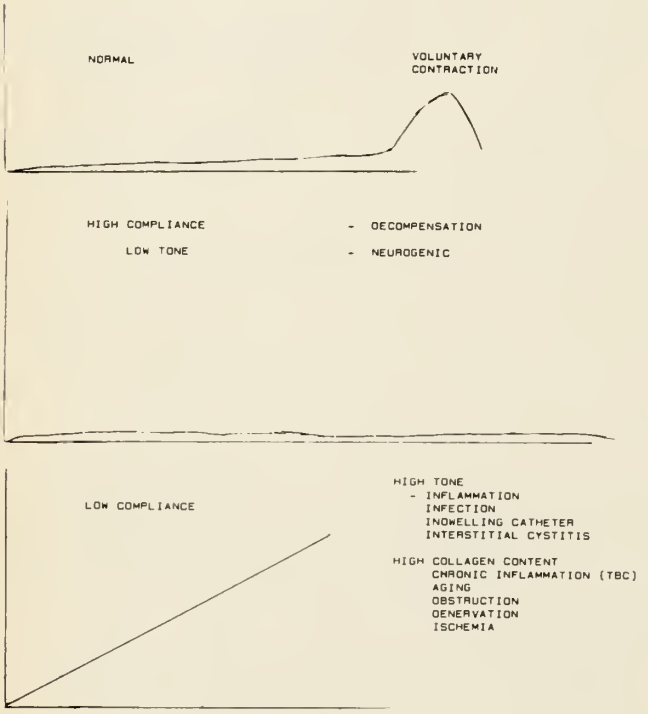


Fig 3. 1. A normal cystometrogram with moderate 5-10cm/H_2O of pressure elevation during filling and a 500 cc capacity; 2. High complicance bladder with increased capacity and no rise in pressure; 3. Low compliance which can be due to either high muscular tone or high collagen content.

B *Urethral Factors.*

1 *Muscular Insufficiency.* Urethral resistance results from a complex association of forces. Muscular deficiency secondary to childbirth injury, lack of exercise, or postmenopausal hypotrophy may affect urethral resistance at several levels.

The weakening of the levator ani muscles may act at two levels. It may provoke a downward urethral and vesical displacement (urethro-cystocele), bringing bladder neck and urethra outside the pelvic cavity.[7] In such a position increase in intraabdominal pressure resulting from straining, coughing, or sneezing is not hormonally transmitted to the urethra as it was when the bladder and urethra were still contained in the pelvic cavity. This factor is usually better corrected by a urethro-cystopexy which aims at repositioning the urethra into the pelvis. We should keep in mind, however, that such an operation is unlikely to correct most of the other factors. The levator ani muscles also contribute between voidings to the normal closure of the vesical neck. Injury to these muscles may result in abnormal urethral length and a variable degree of impairment of the urethral resistance. In our experience, urethral displacement and abnormal vesical neck patency are not always associated to the same degree and both factors should be measured separately, since the therapeutic consequences may differ.

In a parallel way, muscular deficiency may permanently affect the external urethral sphincter. This sphincter is rather flimsy in females and does not appear to play the important role in the maintenance of urinary continence as it does in males. It is conceivable however, that it may be affected to a different degree than levator ani muscles in a childbirth injury. Reinforcing the external urethral spincter is unlikely to be achieved through an operation aimed at the correction of urethral displacement or vesical neck patency.

2 *Other factors of urethral resistance.* a) *Urethral Length.* Functional urethral length in women varies from 25 to 40 mm. We found that nulliparous women presenting with incontinence had a significantly shorter urethra than both the asymptomatic nulliparous group and the incontinent multiparous group, which indicates that urethral length may be a significant predisposing factor in incontinence.[8]

b) *Urethral Compliance.* Urethral tone appears essential to urethral resistance. It can be affected in two opposite ways, rigidity or hyperlaxity. A rigid urethra does not open or close effectively, resulting in both difficulty in voiding and incontinence. Urethral hyperlaxity constitutes an additional factor of incontinence.

The female urethra is mesodermic in origin and is subject to estrogen control as is the vagina. Trophic postmenopausal changes affecting the vagina also affect the urethra, which tends to become rigid. In younger women, the mechanism may be different. The urethra is surrounded by glands very similar to prostatic glands. We believe that nonspecific urethritis is common in females and may lead to increased fibrosis and urethral rigidity. Furthermore, vaginal surgery may cause periurethral fibrosis. We have ob-

served that urethral dilatation was significantly less effective both as to flow rate and symptoms, in patients who had had a previous vaginal hysterectomy and cystocele repair as compared to patients not having had vaginal operations.

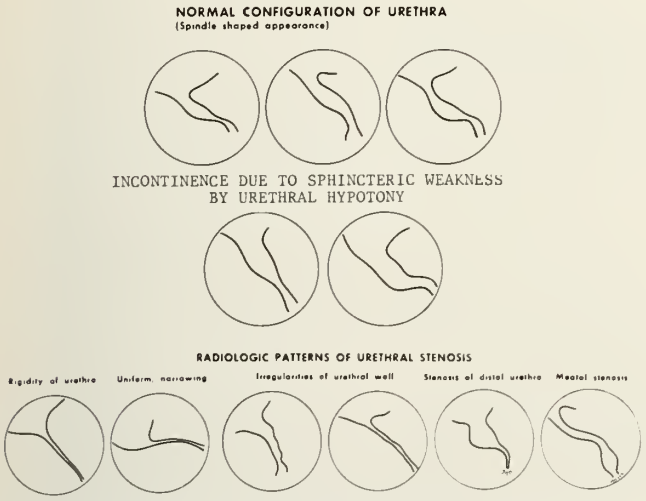


Fig 4. Urethral contours from voiding cystourethrograms taken at peak flow in lateral position.

In a study of 141 cases of incontinence,[6] we found that the flow rate was below normal in 90 cases (63 per cent). A urethral dilatation or a urethrotomy was done in these cases with control of stress incontinence in 72 and 64 per cent respectively of the cases and control of urgency incontinence in 70 and 80 per cent of cases. In the same study, urethral diameters were measured every 5mm on a lateral cysto-urethrography film taken at peak flow. Evidence of rigidity, irregularity, and narrowing could be seen in patients presenting a poor flow rate (Fig 4). A significant correlation was demonstrated between urethral diameters and peak flow rate (Fig 5).

All patients demonstrating a urethra of large diameter on these films had a flow rate at the upper limit of normal. Urethral compliance was then studied by recording urethral pressure with catheters of increasing size; No F12, F18, F20, F24.[9] The rise of pressure was minimal in 8 young, nulliparous, asymptomatic females (Fig 6). In case of abnormal compliance, the initial pressure with a small diameter catheter is lower than normal and increases sharply with the size of the catheter if rigidity is present, or remains low in case of hyperlaxity (Fig 7,8).

When the peak flow is below normal and a urethral dilatation is carried out, the improvement of peak flow averages 15.6 per cent and is parallel to the improvement of the continence and other symptoms such as frequency, urgency, and urethral pain[11] (Fig 9). Such findings point to the importance of uroflowmetry as a screening test in female incontinence (Fig 10).

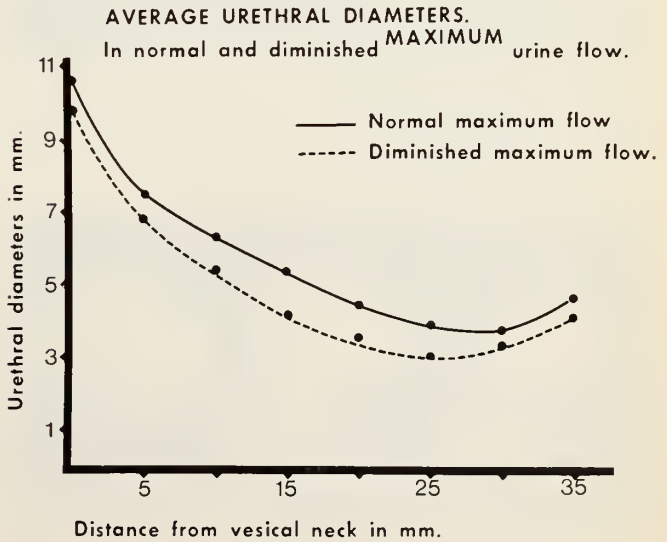
c) *Urethral Hyperreflexia.* A reflex relaxation of the proximal urethra proved to occur normally, immediately preceding voiding (Fig 11).[13] This reflex is largely monitored by the beta adrenergic receptors and is partially suppressed with propranolol. Urethral hyperreflexia may be a factor in incontinence, which may respond to Inderal® (40 mg by mouth for one month). Four of eight patients we treated in this way responded to the treatment.

d) *Degree of urethral moisture and vascularization* are two other factors which we believe are of minor importance in the etiology of female incontinence, but may partly explain some success obtained with estrogen therapy.

The occurrence of incontinence is rarely related to only a single one of these factors. Patient history and physical findings are insufficient for analysis and allow only for a gross differentiation of etiological factors. Even in patients predisposed to incontinence due to the presence of some degree of detrusor hyperreflexia or cystocele, symptoms may not be present, yet the addition of a minor factor such as an abnormal increase in fluid intake may bring on the symptoms.

If the imbalance causing incontinence results from some additional minor factor or factors, it

Fig 5. Although urinary flow may also vary with detrusor contractility, there seems to be a good correlation between peak flow rate and urethral diameter. An abnormally low flow rate pleads in favor of urethral rigidity.



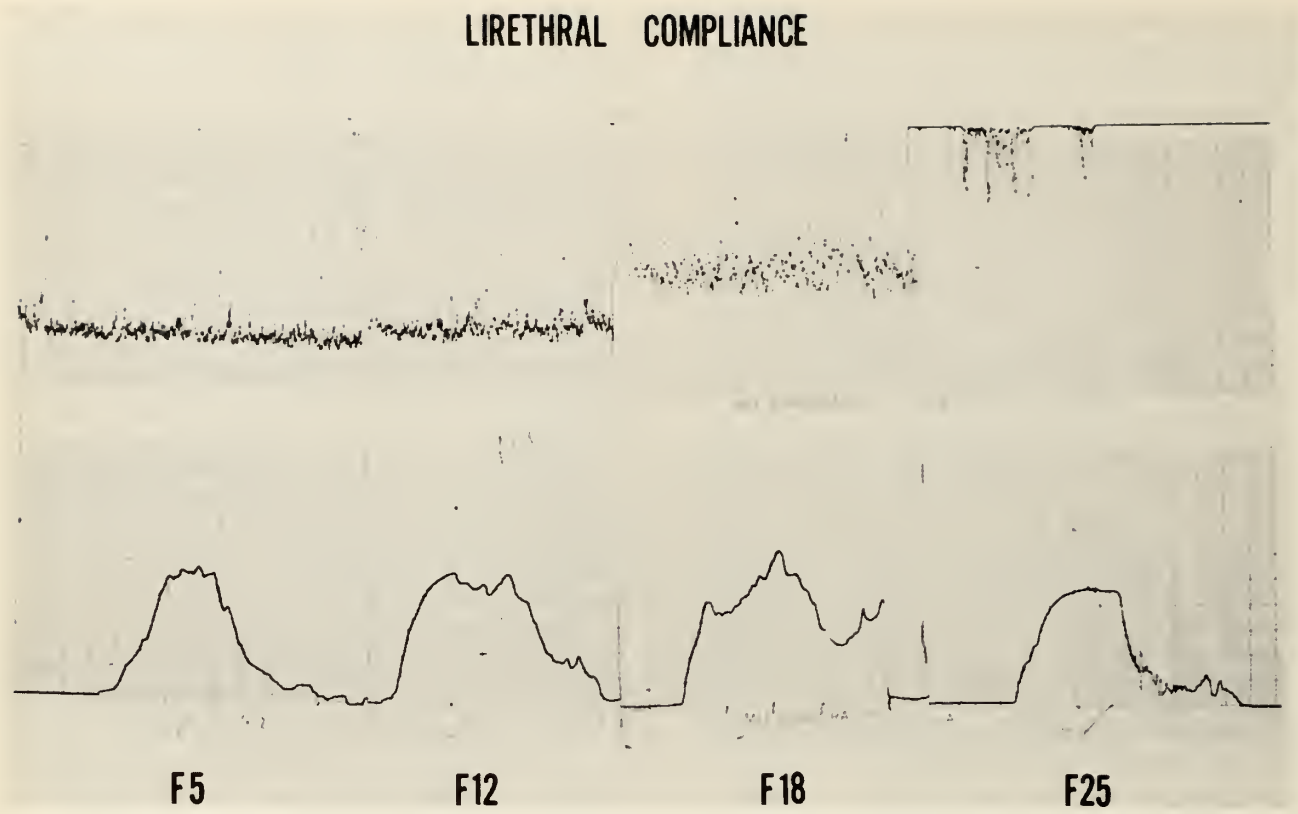


Fig 6. Normal urethral compliance. The urethral pressure is not modified much when measured with a catheter of increasing diameter. (Note perianal EMG in upper part of tracing.)

is logical to assume that it can also be cured with a minor correction of such factors. This probably explains why most treatments, including surgery, yield an average success rate of 60 to 70 per cent. This is also the case with pharmacological agents, alpha-adrenergic agents particularly.[14] The same rate of success is obtained with urethral dilatation. Finally, recent series of systematic reeducation through biofeedback and vaginal electrical stimulation showed a 65 per cent rate of cure.[15] These results are better achieved after a complete urodynamic inventory has been carried out leading to more accurate indications.

In order to choose a plan of treatment, it is indispensable to measure each of the factors by combining urodynamics analysis with a detailed history and physical examination.

Method of Assessment

The method should be guided by the list of vesical and urethral factors which can be involved trying to ascertain the degree of responsibility of each of these factors in the incontinence of a particular patient. No two patients develop incontinence for the same combination of factors.

Assessment of Vesical Factors. The history makes one suspect detrusor hyperreflexia if the patient complains of urgency and frequency of urination. If these symptoms occur only when the patient is up and around and are not present when lying down, it suggests the presence of abnormal vesical neck patency as a cause of detrusor instability. I have seen patients presenting a history of urgency incontinence without evidence of detrusor hyperreflexia on cystometry, and on the contrary I have also seen patients complaining of pure stress incontinence who proved to have a hyperreflexic bladder on cystometry. A cystometric examination is therefore indispensable to acquire the objective evidence of hyperreflexia.

It is better done in the sitting position according to Arnold.[16] Fifty-seven per cent of hyperreflexic bladders will remain undetected if the cystometrogram is performed only in the supine position rather than in sitting or upright positions. The bladder is filled with water at 80 to 100 ml/min. CO_2 cystometry has proven to be

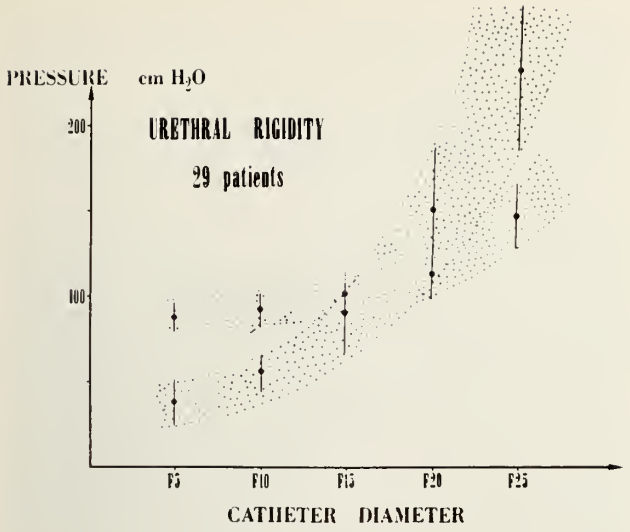


Fig 7. Urethral pressure increases significantly with the size of the catheter utilized to measure it when the urethra is rigid. The pressure is also lower than normal with a catheter of small diameter. The normal values are represented by a group of 8 asymptomatic, young, nulliparous volunteers.

Fig 8. Urethral pressure does not increase with the diameter of the measuring catheter when the urethra is hypotonic. The pressure is lower than normal with a catheter of small diameter. The normal values are from a group of 8 asymptomatic, young, nulliparous volunteers.

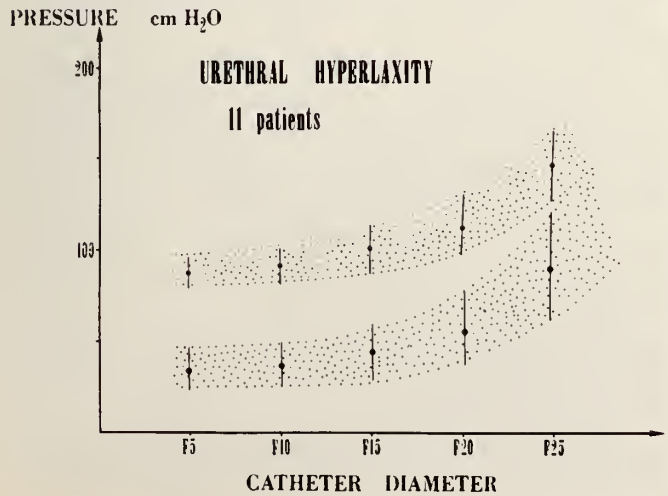


Fig 9. It represents the average improvement of the flow curve following urethral dilatation or urethrotomy. 330 curves obtained prior to the procedure (.....) in 199 patients, and 520 curves were obtained 3 to 18 months following the procedure in the same group of patients (-.-.-). Dimensions are calculated in function of a hypothetical curve of the lower limit of normal. The average improvement of peak flow is 15.6% ($p<.001$). The evolution of flow rate correlates closely with the evolution of symptoms (frequency, nocturia, urethral pain, incontinence).

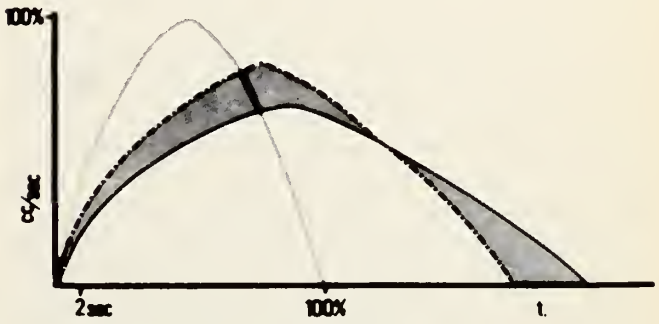
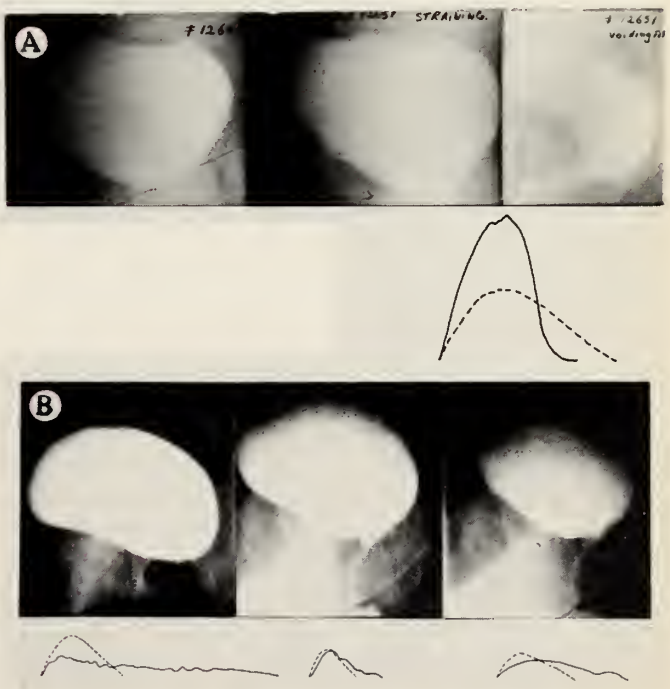


Fig 10. In opposition (A) high flow rate with a radiological aspect of urethral hypotrophy when a colphorraphy was successfully carried out; (B) urethral rigidity with a low flow rate in a 60 year old woman when the incontinence was well controlled by an internal urethrotomy. (The dotted line represents the lower limit of normal for the volume voided.)



unreliable since it lacks reproducibility. Furthermore, gas can escape unnoticed around the catheter, which may mask the rise in pressure due to uninhibited bladder contraction. The demonstration of such contraction is often the main purpose of the test.[17-20] Evaluation of vesical factors also means inquiring about fluid intake and medications, and measuring residual urine, bladder capacity, compliance, and sensation on filling, all provided by catheterization and cystometry.

Assessment of urethral factors. The history helps to determine the degree of possible obstetrical trauma; the type and time of past gynecological surgery; the type of medication taken by the patient; the type of incontinence, whether stress, urgency, or spontaneous; if associated, which type predominates; and how the patient perceives her discomfort. In our series of 141 patients, pure stress incontinence was present as a complaint in 39 patients and urgency incontinence in 28. However, mixed incontinence in 74 represented over 50 per cent of cases.

Physical Examination. The examination concentrates on a number of factors. Among these are the trophic state of the local tissue, whether more or less altered after menopause; the degree of vulvar patency, which reflects the muscular status; shortening of the ano-vulvar distance as a result of past perineal injury; and strength of the levator ani muscles elicited by asking the patient to contract these muscles voluntarily. The latter is graded from 0 to 5. Strong levator ani muscles indicate that urethral displacement, vesical neck patency, and external sphincter contraction may not be markedly impaired. Also noted are the presence and degree of urethrocystocele and rectocele. The urethral meatus is examined to note stenosis or whether covered by remnants of hymen. Both conditions may cause flow turbulence, bacterial regurgitation, and chronic urethritis. It should be emphasized that chronic urethritis may cause urethral rigidity, meatal pain, detrusor hyperreflexia, and lack of sphincter relaxation during voiding. A major etiology of this condition appears to be a reduced caliber of the distal urethra, a caruncle, or remnants of hymen covering the meatus. The size and position of the uterus and condition of the fornices should be noted. Finally, the patient should be asked to cough in order to enable evaluation of the presence and degree of stress incontinence. This is better done in the erect position after 300ml of water have been instilled into the bladder. The Marshall-Krantz maneuver for stress incontinence does not add much to the understanding of the condition.

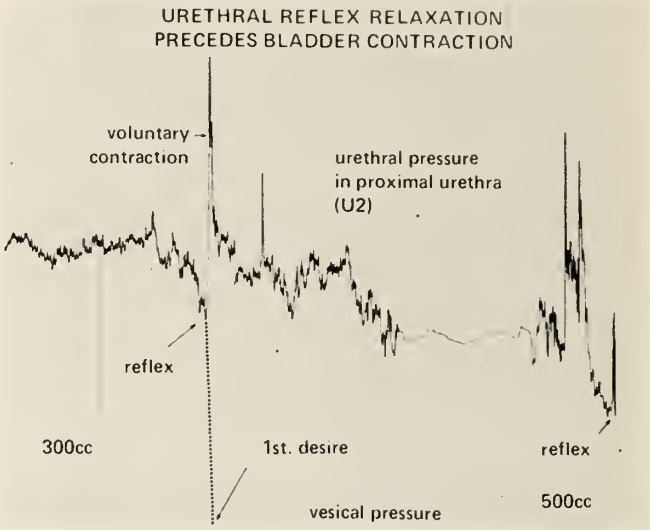
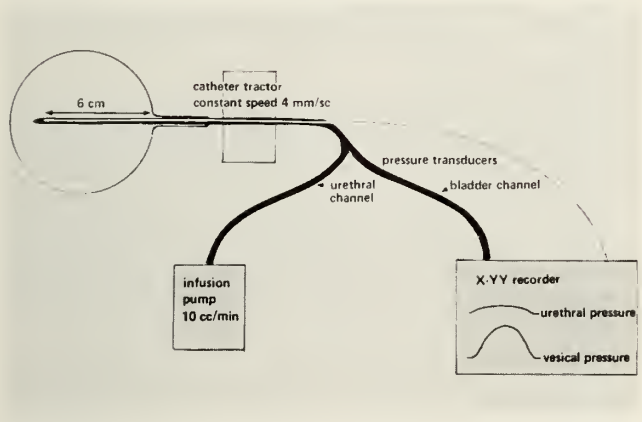


Fig 11. The reflex relaxation of the proximal urethral (upper curve) occurs just before the bladder contraction (lower curve). An exageration of this reflex may be a factor of incontinence.

Urethral pressure profile study allows the analysis of most of the urethral factors (Fig 12).[8,21] A No 10 or 12F catheter is pulled from the urethra at a constant speed, usually 2 mm/second, which is also the speed of the recording paper. It allows measurement of pressure changes at every point of the urethra. It is done with an almost empty bladder. It is first studied at rest. A low maximum closing pressure, below 40cm/H_2O, indicates abnormal urethral tone, which can be due either to rigidity or hyperlaxity. The functional urethral length is recorded. An irregular pressure curve is noted in case of urethral diverticulum, distal urethral stenosis, or iatrogenic urethral stenosis.

It is repeated after the patient is taught to strain in a steady manner (Fig 13) or better, by compressing her abdomen manually. The catheter may have a second channel which allows recording of intravesical pressure simultaneously while the catheter is pulled out. When the urethra is in good pelvic position, most of the increase in intraabdominal and intravesical pressures due to straining is transmitted to the urethra. The degree of reduction of urethral pressure increase during straining measures the amount of urethral displacement and vesical neck descent. It should be noted that measurement should be taken in the proximal urethra, 1 cm before the

Fig 12. Measurement of urethral pressure profile. The catheter is pulled at the same speed as the paper on the recorder. Each mm on the tracing corresponds to the same in the urethra. The catheter is perfused at 10cc/min.



point of maximum pressure. Indeed, straining will usually cause an increase in external sphincter activity. For this reason, transmission defects are more accurately determined in the proximal urethra.

In some cases, straining causes a reduction in urethral length, proportional to the degree of abnormal vesical neck patency (Fig 14). In such instances, urethral displacement cannot be determined by this method, since the transmission of pressure occurs through the vesical neck and no longer across the urethral wall. In some instances, one has to rely upon clinical assessment or cystourethrography to evaluate the degree of urethral displacement.

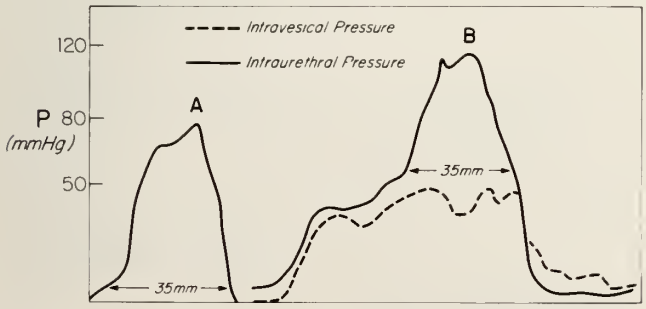
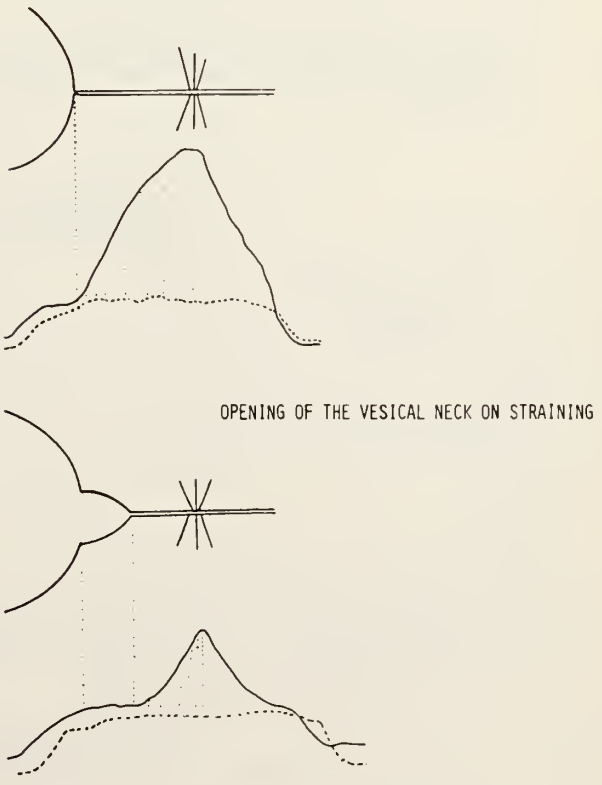


Fig 13. A. Urethral pressure at rest. B. Urethral pressure during constant straining. The rise in pressure in the urethra is the same as the rise in pressure in the bladder. The transmission is normal. The urethra is not abnormally displaced towards the vagina as seen when a urethro-cystocele is present.

A defect in transmission due to urethral displacement can also be evaluated by asking the patient to cough at intervals as the catheter is withdrawn from the urethra. Normally, pressure increase due to coughing should be equal in the bladder and urethra. The urethal pressure is subtracted automatically from the bladder pressure through a third recording resulting in a smooth tracing. The amplitude of the pressure increase due to coughing as observed on this third tracing should be proportional to the degree of displacement. But here also if the vesical neck is patent, the evaluation of the transmission defect will be inaccurate.

The patient is now asked voluntarily to contract her perineal muscles as she was taught to do during the preliminary vaginal examination. The catheter is pulled at the point of maximum pressure and maintained in this position. The strength of the external urethral sphincter is easily evaluated this way. It can reach 150 per cent of the resting pressure. In most normal subjects,

Fig 14. Upper tracing — urethral pressure profile at rest. Lower tracing — urethral pressure profile during straining. The vesical neck is abnormally patent due to levator ani insufficiency resulting in urethral shortening and direct pressure transmission from the bladder to the urethra which is an important factor of stress incontinence.



intraurethral pressure increases due to voluntary contraction average 15 per cent.[21]

Summary of Assessment. An evaluation for female incontinence should begin with a careful history and physical examination. Uroflowmetry measures, both vesical contractions and urethral resistance, is important as a screening test. If the flow rate is at the upper limit of normal, there is a greater probability that the incontinence is due mostly to low urethral resistance. If it is abnormally low, an obstruction has to be ruled out. Following this, the patient is catheterized and the residual urine recorded. A cystometrogram is then carried out in supine, or better, in sitting position, sometimes in both, using water at 80ml/min filling rate. A micturition study immediately follows the cystometrogram. For this a No 5F ureteral catheter is left in the bladder to record intravesical pressure during voiding. Perineal electromyography is recorded simultaneously through two patch electrodes placed around the anal margin. A pressure-flow relationship is established. It may show poor flow and high intravesical pressure indicating obstruction. It may show the presence of an interrupted flow pattern with increased electromyographic activity. The latter indicates the possibility of detrusor-sphincter dysynergia often associated with an upper motor neuron lesion. The micturition study may also demonstrate the absence of detrusor contraction and the need for the patient to strain constantly. Following the micturition study, a urethral pressure profile is obtained.

Finally, if a neurological condition is suspected, it is essential to carry out a neurological examination of the perineum and lower limbs. In such patients a rapid cystometrogram and a sacral nerve conduction study may be indicated.

Treatment Plan

The outcome of the urodynamic inventory is the establishment of a list of factors and their degree of participation in the incontinence. Consequently a logical treatment plan can be proposed in which the most conservative approach is chosen first when proven appropriate. Table 2 summarizes modes of management for each of the factors.

Conclusion

A physio-pathological assessment of the factors involved in female incontinence is now possible through a thorough urodynamic evaluation which appears to us essential for the understanding of the underlying condition. Such an approach should increase the accuracy in the choice of treatment. This in turn leads to improvement of the therapeutic results and many times to conservative management.

In view of the possible complications and rel-

Table 2. Summarizes the methods presently available to control female incontinence. Each factor should be evaluated and treated individually. It is often necessary to treat several factors to correct the incontinence.

	Methods of Treatment		
Factors of Incontinence	**Biofeedback Electrical Stimulation**	**Pharmacology**	**Surgery**
Levator ani deficiency			Urethrocystopexy
— Urethro-vesical displacement	+		Urethrocystopexy
— Vesical neck patency	+		
External sphincter deficiency	+		
Urethral rigidity		Estrogens	Dilatation-Urethrotomy
Urethral hyperlaxity		Alpha-Stimulant	
Urethral hyperreflexia		Propanolol	
Detrusor hyperreflexia			
Obstructive			
— Urethral			Dilatation-Urethrotomy
— Meatal			Dilatation-Meatoplasty
— Vesical Neck			Tur
Inflammatory		Antibiotics Anti-Inflammatory	
Upper motor neuron lesion or idiopathic	Electrical stimulation — Vaginal — Tibial — Sacral	Anticholinergics Imipramine Calcium-blockers	Sacral or pelvic blocks or neurotomies
Polyuria	Control fluid intake		

atively high failure rate of surgical treatment, it is recommended that a complete urodynamic evaluation precede the intervention. An analysis of factors helps to formulate a rational plan of action. In other words, before treating the incontinence, which might require surgery, it appears safer to obtain all the knowledge we can regarding the particular abnormality that we intend to correct.

References

1. Susset, J.G., Dutartre, D., Leriche, A., and Rougemont, M.: Urodynamic assessment of stress incontinence and its therapeutic implications. Surg Gynec Obst, 142(2):343-352, 1976 Mar.
2. Susset, J.G.: Detrusor hyperreflexia in spinal cord lesion, Proceedings of the International Continence Society, Germany.
3. Siroky, M.B., Krane, R.J.: Neurologic aspects of detrusor-sphincter dyssynergia, with reference to the guarding reflex. J Urol, 127:953-957, 1982 May.
4. McGuire, E.J., Lytton, B., Pepe, V. and Kohorn, E.: Stress urinary incontinence. Obst Gynec 47(3):255-264, 1976 Mar.
5. Ramsden, R.D., Smith, J.C., Pierce, J.M., and Ardran, G.M.: The unstable Bladder — Fact or Artefact? Br J of Urol, 49:633-639, 1977.
6. Susset, J.G., Khoukry, I., Schlaeder, G., Gloutier, D. and Dutartre, D.: Stress incontinence and urethral obstruction in women: value of uroflowmetry and voiding urethrography. J Urol 111(3):504-513, 1974 Apr.
7. Enhorning, G.: Simultaneous recording of intravesical and intraurethral pressure. A study on urethral closure in normal and stress incontinent women. Acta Chir Scand suppl 276:1-68, 1961.
8. Susset, J.G. and Plante, P.: Studies of female urethral pressure profile. II. The urethral pressure profile in female incontinence. J Urol 123(1):70-74, 1980 Jan.
9. Regnier, C.H., Susset, J.G., Ghoneim, G.M. and Biancanik P.: A new catheter to measure urethral compliance in females. Normal values. J Urol 129(5): 1060-1062, 1983 May.
10. Susset, J.G., Ghoneim, G.M. and Regnier, C.H.: Abnormal urethral compliance in females diagnosis, results and treatment. J Urol 129(5):1063-1065, 1983 May.
11. Unpublished data.
12. Ghoneim, M.A., Fretin, J., Gagnon, D., and Susset, J.G.: The influence of vesical distension on urethral resistance to flow: the collecting phase. Brit J Urol 47:657, 1975.
13. Ghoneim, M.A., Fretin, J.A., Gagnon, D.J. and Susset, J.G.: The influence of vesical distension on urethral resistance to flow: the expulsion phase. Brit J Urol, 47:663, 1975.
14. Unpublished data.
15. Bourcier, A., J.J. Juras: Urodynomique et Readaptation Enurogynecologie Vigot, Paris 1980.
16. Arnold, E.P.: Cystometry. Personal effects in incontinent women. Uro Int 29:185-186, 1974.
17. Wein, A.J., Hanno, P.M., Dixon, D.O., Raezer, D. and Benson, G.S.: The reproducibility and interpretation of carbon dioxide cystometry. J Urol 120(2):205-206, 1978 Aug.
18. Gleason, D., and Reilly, B.: Gas cystometry. Urologic Clinic of North America 6(1), 1979 Feb.
19. Gleason, D.M., Bottaccini, R.M., Reilly, R.J.: Comparisons of CMGs and urethral profile with gas and water media. Urol 9(2):155-160, 1977 Feb.
20. Hublet, D., Kaechkenbeck, B., and Baker, D.E.: Etude comparative entre la cystometrie al'eau et au gaz. Acta Urologica Belgica 48(4), 1980 Oct.
21. Plante, P. and Susset, J.G.: Studies of female urethral pressure profile. 1. The normal urethral pressure profile. J Urol 123(1):64-69, 1980 Jan.

255 Hope Street
Providence, RI 02906

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY . . . . ANYWHERE

PLUS insurance for . . . .
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

There are three ways to bill

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
#
#
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
				BALANCE FORWARD →		60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/3/85		100.-
9/30/85		Medicare pmt/adj.		-45.-	-8.-	47.-
10/10/85		patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		Pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/adj		-26.-	-5.-	807.-
1/17/86		Court adj.			-3.-	804.-
2/2/86		Medicare pmt/adj		440.-	250.-	114.-

PLEASE PAY LAST AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

BILLED FROM 1-21-86 DATE 2/21/86
BILLED TO 2-20-86 ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

your patients.

Your practice is displayed in a professional manner.

Attach to insurance carrier form and submit for payment from extended benefits.

Words are *printed.* You're not judged by someone else's scribbles.

Services, payments, and adjustments are all clearly described.

Unpaid services are detailed until paid in full.

Patient knows exactly how much he owes and how much insurance company owes. Insurance column optional based on your needs.

Patient year-to-date payment totals.

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

STATEMENT

FED I.D. #00-0000000

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

ACCOUNT NO 12090
STATEMENT DATE 02/21/86

DETACH AND RETURN TOP PORTION WITH YOUR PAYMENT

AMOUNT ENCLOSED $

ATTENDING PHYSICIAN'S STATEMENT

DIAG CODE	SERVICE DATE	PROCEDURE REFERENCE	PATIENT NAME	LOC	DESCRIPTION	CHARGES PAYMENTS ADJ PATIENT	INSURANCE
3624	11/20/85	9003	JAMES	0	INTERMEDIATE EXAMINATION	40.00	
	01/05/86				MEDICARE PAYMENT	-28.00	
	01/05/86				MEDICARE ADJUSTMENT	-5.00	
	01/17/86				NO CO-INSURANCE PAYMENT	0.00	
	01/17/86				COURTESY ADJUSTMENT	-3.00	
	MEDICARE AND CO-INSURANCE HAVE PAID THEIR PORTION OF THIS CLAIM. THE BALANCE IS YOUR RESPONSIBILITY. PLEASE REMIT.						
3624	12/15/85	5637	JAMES	IH	SURGERY		800.00
	02/02/86				MEDICARE PAYMENT		-440.00
	02/02/86				MEDICARE ADJUSTMENT		-250.00
	AWAITING CO-INSURANCE PAYMENT						
	YOUR BALANCE HAS BECOME PAST DUE. PLEASE REMIT.						

CURRENT	OVER 30 DAYS	OVER 60 DAYS	OVER 90 DAYS	OVER 120 DAYS	NEW BALANCE	PATIENT	INSURANCE
.00	4.00	.00	.00	.00		4.00	110.00

ANALYSIS OF PATIENT NEW BALANCE

PATIENT IS RESPONSIBLE FOR "PATIENT NEW BALANCE" SHOWN.

STATEMENT DATE	PATIENT PAY Y T D	ACCOUNT NUMBER
02/21/86	.00	12090

LOCATION CODES
1 OFFICE
2 HOSPITAL IN PATIENT
3 HOSPITAL OUT PATIENT
4 OTHER
5 OTHER
6 OTHER

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY U.S.A.

THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

SAVE THIS DATE

SIXTH ANNUAL ELLA T. GRASSO MEMORIAL CONFERENCE
November 18, 1987

This symposium addresses current clincial problems in gynecologic oncology and research developments that will impact on patient care. It is directed toward obstetricians/gynecologists, medical oncologists, radiation therapists, pathologists, nurses and residents. The symposium is sponsored by the Divisions of Gynecologic Oncology at the Yale University School of Medicine, the Yale Comprehensive Cancer Center and the University of Connecticut School of Medicine.

Location

The Park Plaza
155 Temple Street
New Haven, CT 06511
(203) 772-1700

Guest Faculty

J. Taylor Wharton, M.D.
M. D. Anderson Hospital and Tumor Institute

Peter Wiernik, M.D.
Montefiore Hospital Medical Care

Richard I. Reid, M.D.
Sinai Hospital of Detroit

Howard W. Jones, III, M.D.
Vanderbilt University Medical Center

Maria Merino, M.D.
NIH — NCI

Jeffrey Schlom, M.D.
NIH — NCI

For registration and further information (after AUGUST 1, 1987):

Yale University School of Medicine
Office of Graduate and Continuing Education
New Haven, CT 06510
(203) 785-4578

Single Dose Therapy of Acute Urinary Tract Infection in Women Using Trimethoprim — Sulfamethoxazole: Experience in a Prepaid Internal Medicine Group Practice

Single Dose Therapy in Women is Safe, Effective, and Well Tolerated

Stephen F. Quevedo, MD
Barbara Chace, NP
Susan Kaemmerlen, NP

The first report of single-dose treatment of acute urinary tract infections in women appeared in 1967.[1] Many studies have been published since then using a variety of antibiotic regimens. Most experience, however, has been with trimethoprim — sulfamethoxazole or amoxicillin.[2-8] Cure rates have been somewhat better for the former drug, with results approaching that of conventional seven- to ten-day therapy.[9,10]

During the past decade clinical studies have clearly demonstrated that the success of single-dose therapy is dependent upon whether the infection is localized to the bladder, or also involves the upper urinary tract. Pooled data show that ninety per cent or more of women with lower urinary infection are cured by single-dose therapy, compared with a fifty per cent success rate in patients with upper urinary tract involvement.[9,11] The percentage of upper urinary tract involvement at presentation varies widely depending upon the patient population studied, from eight per cent in a West Coast, prepaid health plan to sixty-three per cent in an urban emergency room population.[3]

It follows that single-dose therapy of acute urinary tract infections in women is most appropriate in patient populations with relatively low percentages of upper tract involvement. Unfortunately, techniques for rapidly determining this are not readily available to the clinician. We decided, therefore, to study prospectively our experience with single-dose therapy, utilizing trimethoprim-sulfamethoxazole.

Stephen F. Quevedo, MD, is in the practice of internal medicine with the Rhode Island Group Health Association.

Barbara Chace, NP, is a nurse practitioner with the Department of Internal Medicine at the Rhode Island Group Health Association.

Susan Kaemmerlen, NP, is a nurse practitioner with the Department of Internal Medicine at the Rhode Island Group Health Association.

From the Rhode Island Group Health Association, Department of Internal Medicine.

Methods

Between May 1982 and December 1985, seventy-nine consecutive women presenting with symptoms of acute urinary tract infection (dysuria with frequency or urgency) to one internal medicine team at Rhode Island Group Health Association (two physicians and two nurse practitioners) were eligible for the study. Patients were not eligible if they had any of the following: diabetes, an oral temperature of greater than 100.4°F, flank pain or costovertebral angle tenderness on examination, rigors, pregnancy, known anatomic abnormalities of the urinary tract, renal insufficiency, allergy to sulfonamides or trimethoprim, a history of more than one urinary tract infection in the preceding twelve months, or obvious vaginitis.

Patients were entered into the study who had significant pyuria (defined as greater than, or equal to 10 leucocytes per high power field of centrifuged urine) and who had greater than or equal to 10^4 gram negative or 10^5 gram positive organisms per milliliter on culture.

Patients were treated with a single-dose of two double-strength Bactrim® tablets (total of 320 milligrams of trimethoprim and 1600 milligrams of sulfamethoxazole). They were asked to return in one week for a follow-up culture and to call immediately for persistent or recurrent symptoms.

Three months after treatment all charts were reviewed, and patients were interviewed by telephone to determine whether they had been treated for recurrent symptoms either within or outside of the Rhode Island Group Health system and to monitor for side effects of therapy.

Relapse was defined as either a positive culture with the same organism (including the same antibiotic sensitivity pattern) at routine follow-up, or by recurrent symptoms with the same organism cultured during the three month post-treatment period. Reinfection was defined as recurrent symptoms with culture of a different organism, or of the same organism with a different antibiotic sensitivity profile.

Patients with relapsed infection or reinfection were treated with two weeks of conventional antibiotic therapy.

Results

A total of fifty-six women (seventy-one per cent) met the criteria for urinary tract infection. Of these, thirty-eight (sixty-eight per cent) complied with our request for a follow-up culture. These were obtained a mean of 10.3 days after treatment (range four — twenty-four days). Chart review was performed in all fifty-six patients, and fifty-four patients (ninety-six per cent) were interviewed by telephone.

By the end of the study period six patients had relapsed (eleven per cent), a mean of eleven days after initial therapy (range six to twenty-one days). An additional three patients experienced reinfection a mean of fifty-two days after the initial infection (range forty-four to fifty-six days). These three patients were considered cures.

The bacteria initially cultured were predominantly Escherichia coli, with lesser numbers of Staphylococcus epidermidis or saprophyticus, Proteus species, and other isolates. A similar bacteriologic distribution was noted in the patients who relapsed (Table 1).

When the relapse and cure groups were compared with regard to mean age, length of symptoms, number of urinary infections in the preceeding year, and colony count on initial culture, no statistically significant differences were observed (Table 2). None of the relapsed or reinfected patients developed signs or symptoms of pyelonephritis during the study period. No patient developed a manifestation of drug allergy, such as rash or stomatitis.

Table 1. Bacteriology (% of Isolates).

Organism	Initial	Relapses
Escherichia coli	71	67
Staph. epidermidus or saprophyticus	13	17
Proteus Species	5	17
Unspecified Gram Neg.	4	
Citrobacter	2	
Serratia	2	
Klebsiella pneumoniae	2	
Alpha-Streptococcus	2	

Table 2. Patient Characteristics — Mean (Range).

	Cures	Relapses	Statistical Significance*
Age (Years)	36 (18-72)	40 (25-78)	N.S.
Length Symptoms (Days)	2.2 (0.5-3)	1.3 (0.5-10)	N.S.
Number UTI's in Past Year	0.2	0	N.S.
Colony Count > 10^5 On Culture (Percent of Total)	58	80	N.S.

* CHI Squared Analysis

Discussion

In order to assess the efficacy of a given therapy, it is essential to define the disease under treatment as precisely as possible. The bacteriologic criteria for the diagnosis of gram negative urinary tract infection in women is no longer culture of greater than or equal to 10^5 organisms per milliliter of urine, as convincingly demonstrated by Stamm and his colleagues.[12] However, commercial laboratories will not routinely isolate as few as 100 organisms per milliliter, and diagnostic sensitivity predictably decreases with the colony count. We therefore used a criterion of greater or equal to 10^4 organisms per milliliter for the diagnosis of coliform urinary tract infection, which gives both a diagnostic sensitivity and specificity of greater than ninety per cent.[13] As gram positive urinary infections have not been as extensively studied, we defined gram positive infection by the traditional 10^5 organism per milliliter criterion.

Our definition of pyuria is also the traditional one. While measurement of leukocytes in unspun urine by counting chamber may correlate better with actual leukocyte excretion,[14] this technique is not yet widely used in clinical practice.

Utilizing the above criteria, seventy-one per cent of our initial group fulfilled our definition of acute urinary tract infection, a percentage which compares favorably with reports in the literature (51 to 76 per cent).[3-6,8] Our cure rate of eighty-nine per cent is consistent with most previous studies using trimethoprim-sulfamethoxazole. A weighted average of six of the largest studies gives a cure rate of ninety per cent.[10] These results suggest that a relatively small percentage of our population has upper urinary tract involvement at presentation. None of our patients developed progressive infection with development of pyelonephritis, a finding also consistent with the literature experience.[2-8,15]

While we did not screen for mild drug-related side effects, such as nausea or vaginitis, none of our patients developed severe stomatitis or drug rash. Review of the published data on the incidence of side effects of single dose versus conventional therapy reveals a clearly decreased incidence in the single dose groups.[10,15]

Our data indicate that in our patient population, single-dose therapy using trimethoprim-sulfamethoxazole of acute urinary tract infection in women is safe, effective, and well tolerated. Taking into account simplicity, potentially increased patient compliance, and a probable decrease in adverse drug reactions, we feel it is the treatment of choice in this population and in others with similarly low percentages of upper urinary tract involvement. Indeed, a recent decision-analysis study[10] using assumptions of effectiveness quite consistent with our data showed that single-dose therapy reduces both symptom-days (days with symptoms from initial infection, relapse, or drug side effect) and cost.

Acknowledgments

The authors are indebted to: Stephen H. Zinner, MD, Head, Division of Infectious Disease, Roger Williams General Hospital, for his review of the manuscript and his helpful suggestions, and Mary Lou DeCiantis, PhD, for statistical assistance.

References

1. Gruneberg RN, Brumfitt W: Single-Dose Treatment of Acute Urinary Tract Infection: A Controlled Trial. Br Med J 3:649-651, Sep 1967.
2. Fang L, Tolkoff-Rubin N, Rubin R: Efficacy of Single-Dose and Conventional Amoxicillin Therapy in Urinary Tract Infection Localized by the Antibody-Coated Bacteria Technic. N Engl J Med 298:413-416, Feb 1978.
3. Rubin R, Fang L, Jones S et al: Single-Dose Amoxicillin Therapy for Urinary Tract Infection. JAMA 244:561-564, Aug 1980.
4. Savard-Fenton M, Fenton B, Reller LB et al: Single-Dose Amoxicillin Therapy with Follow-up Urine Culture. Am J Med 73:808-813, 1982.
5. Buckwold F, Ludwig P, Harding G et al: Therapy for Acute Cystitis in Adult Women — Randomized Comparison of Single-Dose Sulfisoxazole vs. Trimethoprim-Sulfamethoxazole. JAMA 247:1839-1842, Apr 1982.
6. Schultz H, McCaffrey LA, Keys T et al: Acute Cystitis: A Prospective Study of Laboratory Tests and Duration of Therapy. Mayo Clin Proc 59:391-397, Jun 1984.
7. Hooton T, Running K, Stamm W: Single-Dose Therapy for Cystitis in Women — A Comparison of Trimethoprim-Sulfamethoxazole, Amoxicillin, and Cyclacillin. JAMA 253:387-390, Jan 1985.
8. Tolkoff-Rubin N, Wilson M, Zuromskis P et al: Single-Dose Amoxicillin Therapy of Acute Uncomplicated Urinary Tract Infections in Women. Antimicrob Agents Chemother 25:626-629, May 1984.
9. McCabe J, Hamilton G: Single-Dose Antibiotic Therapy of Urinary Tract Infection: Is it Appropriate in the Emergency Department? Ann Emerg Med 13:432-439, Jun 1984.
10. Carlson K, Mulley A: Management of Acute Dysuria — A Decision — Analysis Model of Alternative Strategies. Ann Intern Med 102:244-249, Feb 1985.
11. Sheehan G, Harding G, Ronald A: Advances in the Treatment of Urinary Tract Infection. Am J Med 76(5A):141-147, May 1984.
12. Stamm W, Counts G, Running K et al: Diagnosis of Coliform Infection in Acutely Dysuric Women. N Engl J Med 307:463-468, Aug 1982.
13. Smith G, Brumfitt W, Hamilton-Miller J: Diagnosis of Coliform Infection in Acutely Dysuric Women (Letter). N Engl J Med 309:1393, 1983.
14. Stamm W: Measurement of Pyuria and its Relation to Bacteriuria. Am J Med 75:53-58, Jul 1983.
15. Fihn S: Single-Dose Antimicrobial Therapy for Urinary Tract Infections (Editorial). J Gen Intern Med 1:62-65, 1986.

530 North Main Street
Providence, Rhode Island 02904

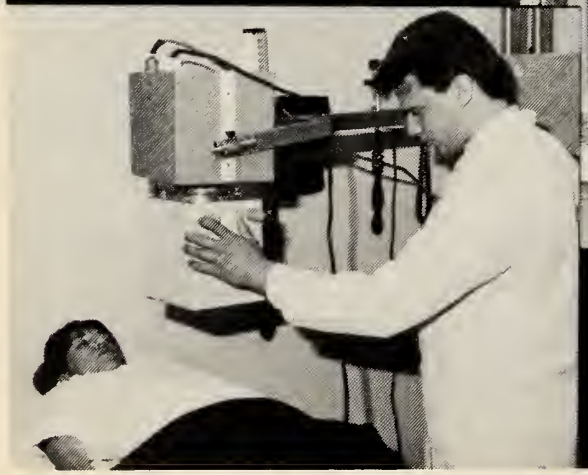
We've become the largest full service medical lab in Rhode Island... *because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Rhode Island Physicians' Recognition and Reporting of Adverse Drug Reactions

Increased Physician Participation in Post-Marketing Surveillance Will Lead To Greater Understanding of Adverse Drug Reactions

H. Denman Scott, MD, MPH
Sara E. Rosenbaum, PhD
William J. Waters, PhD
Avery M. Colt, MA
Lisa G. Andrews, MBA
John P. Juergens, PhD
Gerald A. Faich, MD, MPH

Background

Virtually every drug used in treatment of medical conditions has adverse reactions. For most drugs, the toxicity profile is well known, and the adverse effects are relatively mild. Adverse reactions and contraindications are defined in package inserts and physician desk reference publications. In some instances, adverse effects are relatively severe, but may be outweighed by benefits of treatments. Anticipating and responding to adverse drug reactions (ADRs) is a usual part of medical practice.

H. Denman Scott, MD, MPH, is Director of the Rhode Island Department of Health, Providence, Rhode Island.

Sara E. Rosenbaum, PhD, is Project Director for the Adverse Drug Reaction Reporting Project, Rhode Island Department of Health, Providence, Rhode Island

Lisa G. Andrews, MBA, is the former Project Director for Adverse Drug Reaction Reporting Project, Rhode Island Department of Health, Providence, Rhode Island.

William J. Waters, PhD, is the Assistant Director for the Health Policy with the Rhode Island Department of Health, Providence, Rhode Island.

John P. Juergens, PhD, is Project Manager at the Office of Epidemiology and Biostatistics, Food and Drug Administration, Rockville, Maryland.

Avery M. Colt, MA, is the Director of Corporate Development at Rhode Island Health Services Research, Inc., Providence, Rhode Island.

Gerald A. Faich, MD, MPH, is Director at the Office of Epidemiology and Biostatistics, Food and Drug Administration, Rockville, Maryland.

Potential problems for physicians and patients occur when toxicity profiles have not yet been completely identified. Although all new pharmaceuticals must be tested for safety and efficacy as conditions of United States Food and Drug Administration (FDA) approval, clinical trials cannot identify all possible adverse effects. The usual trial is too small to identify less common adverse reactions, and the duration of trials is too short to identify latent effects, ie, those which take several years to appear. Additionally, the selection process for subjects in clinical trials often eliminates patients who may be at particular risk for experiencing adverse reactions, eg, children, pregnant women, persons with several chronic diseases, and persons taking multiple medications.

There is a recognized need, therefore, to continue monitoring drug use even after the product has been approved. This *post-marketing surveillance* function is the responsibility of the FDA.

As currently constituted, post-marketing surveillance involves four steps:

- *Reporting.* The FDA receives reports of serious or unexpected adverse health events which occurred during drug use.
- *Analysis.* Reports are entered in a computerized data-base, which is analyzed on a continuous basis to identify suspicious patterns of drug-disease association.
- *Investigation.* When suspicious patterns of drug-disease association are identified, the FDA conducts (or requires the manufacturer to conduct) epidemiologic and investigative studies to determine if there is a causal relationship between drug use and adverse events.
- *Remedial Action.* If a causal relationship is found, the FDA: (1) informs the physician community, (2) may require changes in the package insert information, and (3) may, in the worst cases, require removal of the drug from the market.

The entire process depends upon the FDA receiving reports from physicians. The focus is on *serious or unexpected* events following drug use. Proof of a causal relationship between drug use and adverse event is not a requirement for reporting. Indeed, it is generally impossible for an individual physician to establish a cause-effect relationship. The FDA provides a straightforward form for physicians to use, which requires three to five minutes to fill out. Patient name is not reported and confidentiality of physician identification is protected.

It has been estimated that adverse drug reactions cause approximately 30,000 deaths and 1.5 million hospital admissions annually.[1,2] In recent years, however, the FDA has received approximately 40,000 reports of suspected adverse drug reactions, of which 10 per cent come directly from physicians, and the remainder through reports from manufacturers and other sources. In other words, the level of physician reporting is a fraction of the total number of reportable events.

The FDA is not only anxious to increase total reporting of suspected adverse drug reactions, but also the proportion of reports which come directly to the agency from practicing physicians. In 1970, direct reports from physicians were only one per cent of reports received; yet this direct physician input accounted for 24 per cent of all new verified adverse drug reactions in that year.[3] Most importantly, a recent study found spontaneous reports from physicians more effective in identifying new adverse drug reactions than some extremely large, well-organized, costly, major phase IV clinical trials, which used study cohorts of up to 22,000 subjects.[4]

In short, direct physician reports of suspected adverse drug reactions have proven very effective in monitoring drug safety. The FDA needs continued and enhanced cooperation from physicians to strengthen the post-marketing surveillance process and to protect patients from the consequences of adverse drug reactions.

Rhode Island Survey

As part of a pilot project funded by the FDA, the Rhode Island Department of Health has conducted a survey of Rhode Island physicians to determine their experience with adverse drug reactions. In January 1986, questionnaires were mailed to 1,585 practicing physicians in the state. Responses were received from 74 per cent or from a total of 1,167 respondents. The distribution of primary specialties among respondents is shown in Table 1.

A summary of survey results is presented below.

1. *Number of Adverse Drug Reactions (ADRs) Reported in Rhode Island.* Respondents were asked how many patients they had seen in the past year with symptoms which they suspected had resulted from use of therapeutic drugs, regardless of severity. They were also asked how many patients they had seen in the past year with more serious adverse drug reactions defined as follows:

FATAL — resulted in patient death, or

SEVERE — required inpatient stay or resulted in significant disability, or

MODERATE — required treatment in emergency room or physicians office.

Responding physicians reported having seen a total of 27,000 suspected ADRs of all types in the past year. While many of these were of a minor nature, respondents reported they observed a total of 61 suspected fatal ADRs, 1,075 suspected severe ADRs, and 8,344 suspected moderate ADRs.

If one assumes that non-respondents to the survey saw suspected ADRs in the same proportion as respondents, there were approximately 36,000 suspected ADR of all types in the state in 1985, and approximately 2,000 fatal or severe suspected ADRs.

According to the FDA, an average of 55 reports of suspected adverse drug reactions were received from Rhode Island each year in the decade 1976-1985. These reports were from all sources, not just direct reports to the FDA from physicians. A total of 11 direct reports from physicians were received in 1985. Thus, using only the fatal and severe ADRs reported in the survey, we can estimate that less than one per cent of suspected serious ADRs are reported directly to the FDA.

2. *Who Observed Serious Suspected ADRs.* Twenty-nine respondents (2.5 per cent) reported seeing a fatal suspected ADR, 266 (23.3 per cent) reported seeing a severe suspected ADR; and 656 (58.1 per cent) reported seeing a moderate suspected ADR. Put another way, respondents reported seeing, in 1985, an average of 0.05 fatal suspected ADRs per physician, 0.9 severe suspected ADRs per physician, and 7.2 moderate suspected ADRs per physician.

Owing to the larger numbers involved, the severe and moderate suspected ADRs were analyzed in greater detail. Table 1 shows the distribution by specialty, of physicians who reported observing suspected ADRs. It can be seen from Table 1 that suspected ADRs were reportedly observed by physicians in almost all major specialties. The percentage of each major specialty who reported observing one or more suspected ADRs during 1985 is shown in Table 2. It can be seen that reported exposure was particularly high for physicians practicing emergency room medicine, oncology, internal medicine, allergy and dermatology, cardiology, psychiatry, and family practice medicine (Table 2). When the average number of ADRs per physician was calculated for each major specialty (Table 2), the largest reported observation rate, was found in physicians practicing emergency room medicine, psychiatry, cardiology, internal medicine, and oncology.

The reported observation of both severe and

Table 1. Distribution by Specialty of all Respondents and Respondents who Reported Observing Suspected ADRs.

	Total Respondents		Observers of ADRs: SEVERE ADRs		Observers of ADRs: MODERATE ADRs	
	No.	*% of total*	*No.*	*% of total*	*No.*	*% of total*
Internal medicine	154	13.2	59	22	116	18
Psychiatry	98	8.4	27	10	55	8
Family Practice	62	5.3	17	6	44	7
Emergency Room Medicine	38	3.3	19	7	33	5
Radiology/Pathology/Anesthesiology	121	10.4	14	5	34	5
Cardiology	35	3.0	13	5	22	3
Pediatrics	91	7.8	8	3	52	7
General Surgery	71	6.1	9	3	33	5
Specialty Surgery	80	6.9	11	4	36	6
Allergy/Dermatology	29	2.5	9	3	23	4
Oncology	9	0.8	5	2	5	1
Obstetrics/Gynecology	72	6.2	3	1	36	6
General Practice	35	3.0	3	1	22	3
Geriatrics	5	0.4	1	0.4	4	0.6
Other	207	15.8	57	22	112	17
No Information	60	5.1	11	4	29	4
	1167	~100%*	266	~100%*	656	~100%*

* May not equal 100% due to rounding

Table 2. Reported Observation of Suspected ADRs for Each Major Specialty. Per Cent of Each Specialty Observing Suspected Severe and Moderate ADRs and the Average Number per Physician.

Specialty	Per Cent Who Saw One or More ADR		Average Number per Physician	
	Severe	Moderate	Severe	Moderate
Emergency Room Medicine	50*	87	2.0*	30.0
Oncology	56	56	2.1	8.2
Internal Medicine	38	75	1.9	12.5
Allergy/Dermatology	31	79	0.9	14.8
Cardiology	37	63	2.0	9.5
Psychiatry	28	56	2.2	11.1
Family Practice	27	71	0.4	7.5
General Practice	9	63	0.2	4.5
Pediatrics	9	57	0.2	3.0
Specialty Surgery	14	45	0.2	2.0
General Surgery	13	47	0.2	4.1
Obstetrics/Gynecology	4	50	0.1	2.8
Radiology/Pathology/ Anesthesiology	5	28	0.3	3.4

* For example, 50% of respondents who practiced emergency room medicine saw 1 or more severe ADRs during 1985. Respondents who practiced emergency room medicine saw an average of 2.0 severe ADRs during 1985.

moderate ADRs increased in proportion to the number of prescriptions written per week (data available on request).

3. *Physician Response to a Suspected Serious Adverse Drug Reaction.* Respondents were asked to indicate what actions they thought they would take if they suspected that one of their patients experienced a fatal, severe or moderate adverse drug reaction.

Of particular interest was the percentage of physicians who would report to the FDA directly. When faced with a suspected fatal ADR, 50 per cent of respondents said they would report directly to the FDA, 42 per cent for a severe reaction, and only 14 per cent for a moderate suspected ADR (Table 3). However, physicians practicing emergency room medicine, family practice medicine, general practice medicine, and surgery were generally less likely to report suspected ADRs to the FDA (data available on request).

Respondents indicated that they would be more likely to submit a report of a fatal ADR to the Department of Health rather than to the FDA. For severe and moderate ADRs, respondents would be equally likely to submit a report to the Department of Health as the FDA (Table 3).

The most frequent action indicated by respondents for all types of suspected ADRs was to consult with another physician (Table 3).

4. *Reasons Physicians May Hesitate in Reporting Directly to the FDA.* Physician familarity with the FDA's voluntary reporting system appears to be a serious problem. Only 55 per cent of respond-

Table 3. Respondents Reported Action in Response to a Suspected Adverse Drug Reaction.

	Type of Suspected ADR		
	Fatal	Severe	Moderate
	(% of Respondents)		
Report to FDA	50	42	14
Consult Other MD	63	67	47
Consult Pharmacist	45	47	33
Contact Drug Detail Representative	24	25	20
Contact Manufacturer Directly	47	35	13
Report to Hospital Review Committee	52	41	17
Report to Department of Health	70	42	14
No Action	2	4	32
	Not Additive*	Not Additive*	Not Additive*

* Respondents indicated one or more actions

Table 4. Reasons Respondents May Hesitate to Report a Suspected ADR to the FDA.

	Total Respondents (% of Total Respondents)	Reported Observers of ADRs		
		Fatal	Severe	Moderate
		(% of Observers)		
Reporting wouldn't occur to me	20	31	27	24
Don't know how	21	10	20	24
Don't have time	5	10	11	7
Couldn't be sure drug caused reaction	28	38	34	32
Reaction was expected	24	48	38	29
Concern over legal liability	8	7	5	8
Don't have forms	38	35*	41	43
None, I wouldn't hesitate	40	21	29	34
	Not Additive†	Not Additive†	Not Additive†	Not Additive†

* For example, 35% of those physicians who reported observing a fatal ADR indicated that they might hesitate reporting a suspected ADR to the FDA because they don't have forms.

† Respondents gave one or more reasons.

ents said they were familiar with the reporting system. Furthermore, only 40 per cent of respondents were familiar with the specific report forms and guidelines.

Respondents were asked to indicate the reasons that might make them hesitate to report a suspected serious ADR directly to the FDA. The major reasons for hesitation cited by respondents (Table 4) were "lack of FDA report forms," "uncertainty the drug caused the reaction," "don't know how," "reaction expected," or "it wouldn't occur to me."

Encouragingly, serious factors, less amenable to change, such as, "concern over legal liability," "lack of time," and "not my responsibility" were considered important by only a minority of respondents (Table 4).

Potential reasons for hesitation given by respondents who reported observing one or more fatal, severe, or moderate ADR is also shown in Table 4. Among those observing ADRs, lack of certainty of a cause-effect relationship and expectation of the reaction both achieved greater significance in terms of reporting hesitation (Table 4). Additionally, when compared to respondents as a whole, a greater percentage of observers of ADRs said that reporting would not occur to them. Likewise, a smaller percentage of observers said they would not hesitate to submit a report (Table 4).

Discussion

A major purpose of the Rhode Island survey was to try to identify any impediments that exist to prevent physicians from voluntarily reporting ADRs to the FDA. Only a minority of respondents claimed they would submit a report to the FDA in the hypothetical event that they encountered a suspected severe or moderate ADR. This indicates that many either may underestimate the value of these events for the post-marketing surveillance of drugs or, alternatively, that they are unaware of the reporting system and the channels used to submit reports. The study supports both propositions. A significant percentage (20 per cent) of respondents said reporting would not occur to them, and only a minority (40 per cent) are familiar with the report forms and guidelines of the FDA's reporting system (Section 4).

A comparison of the number of respondents who said they would submit a report to the FDA and of the number of reports that the FDA currently receives from Rhode Island sources indicates that factors deter those who intend to participate from actually doing so. Optimistically, the survey identifies availability of report forms and familiarity with the system as major inhibitory factors. Also, many respondents indicated that they felt that reports should only be submitted when they were certain of the drugs contribution. As discussed earlier, it is generally impossible for an individual physician to establish causality. Reports should be submitted whenever a physician suspects that a drug has contributed to a serious clinical event.

Suspected serious ADRs are perhaps most simply defined as any event suspected of being drug related, that results in a change in the course of treatment of a patient. Reports of these events are essential in order to obtain the full toxicity profile of a drug and to identify any particularly

sensitive groups of individuals. Several thousand suspected serious ADRs were observed in Rhode Island in 1985. As new and more powerful drugs become available one must speculate that this number can only increase. The Rhode Island survey confirms that the FDA's voluntary reporting system is presently greatly underutilized. Less than one percent of the fatal and severe ADRs identified by this study were reported to the FDA.

The Rhode Island Department of Health is currently conducting a federally sponsored campaign to increase physician participation in the FDA's voluntary reporting system. Reporting kits consisting of report forms and reporting guidelines have been distributed to all practicing physicians in the state. Educational sessions have been conducted and continue to be scheduled throughout the state. In addition, educational and promotional material is mailed to all practicing physicians at regular intervals. The survey indicates that the campaign should be successful, since it directly addresses the major reporting impediments identified by respondents.

An increased physician participation in the post-marketing surveillance process will ultimately lead to a greater understanding of adverse drug reactions. This in turn will enable physicians to use prescription medication in a safer and more effective manner.

Acknowledgments

The authors wish to acknowledge the valuable contributions of the ADR Project Advisory Committee: Jay S. Buechner, PhD, Charles Hachadorian, RPh, Richard A. Keenlyside, MBBS, Thomas Della Torre, MD, Nancy Mirto, Norman Campbell, PhD, JD, Steven A. Wartman, MD, PhD, Louis P. Jeffrey, ScD, John W. Norton, and Ernest Oliver, RPh.

References

1 Melmen VL: Preventable Drug Reactions — Causes and Cures. New Eng J Med 284:1361-1368, 1971.

2 Bosen MM: The Elderly and Drugs — Problems Overview and Program Strategy. Public Health Rep 92:43-48, 1977.

3 Rossi AC and Knapp DE: Discovery of new adverse drug reactions: A review of the Food and Drug Administration's spontaneous reporting system. JAMA 252:1030-1033, 1984.

4 Rossi AC, Knapp DE, Anello C et al: Discovery of adverse drug reactions: A comparison of selected iv studies with spontaneous reporting methods. JAMA 249:2226-2228, 1983.

LOOKING FOR AN INVESTMENT WITH TAX ADVANTAGES?

We can point you in the right direction.

COMPASS-LIFE

This powerful financial planning opportunity helps you build your assets *tax free** while you protect your heirs.

Compass-Life is single premium variable life insurance from Massachusetts Financial Services, America's oldest mutual fund organization, and Sun Life (U.S.), a subsidiary of one of the world's largest life insurers.

*If your Compass-Life contract is held for your lifetime, then no income taxes will ever be payable. If your contract is cancelled, taxes will be due on any amounts above your original investment. Cash value and death benefit will be reduced by any loans outstanding.

William C. Martin, Second Vice President, Financial Consultant
Shearson Lehman Brothers Inc.
180 Westminster Mall, 2nd Fl., Providence, RI 02903
401-272-1160 1-800-556-7362

Please send me more complete information on Compass-Life, including a prospectus describing all charges and expenses, which I should read carefully before I invest or send money.

Name_____

Address_____

City_____ State_____ Zip_____

Home phone_____ Bus. phone_____

SEMI-ANNUAL CALENDAR OF CONTINUING MEDICAL EDUCATION EVENTS

NOTE: Lectures and courses are listed by the date, sponsor, topic, speaker, and telephone number for additional information. Please call the contact number for specific information about the program.

JULY

15 The Memorial Hospital, "Update on Newer Antibiotics," Richard Gleckman, MD, Professor of Medicine, University of Massachusetts, Worcester, (401)722-6000, ext. 2246.

29 The Memorial Hospital, "Gastrointestinal Bleeding," Robert Burakoff, MD, Chief of Gastroenterology, Winthrop University Hospital, Mineola, New York, Professor of Medicine, State University of New York (Stonybrook), (401)722-6000, ext. 2246. Sponsors: The Memorial Hospital, Smith Kline, French.

SEPTEMBER

TBA Emma Pendleton Bradley Hospital, Child Psychiatry Grand Rounds, Speakers to be announced, time: 11:00-12:30 pm, (401)434-3400, ext. 153.

9 Brown University Program in Medicine, "Infectious Diseases of the Diabetic Foot," speaker to be announced, Sponsor — Roger Williams General Hospital, (401)863-3337.

14 General Hospital, Rhode Island Medical Center, Topics on the Central Nervous System (series), Stanley M. Aronson, MD, University Professor of Medical Science, Brown University Medical Program, (401)464-3456.

15 General Hospital, Rhode Island Medical Center, "Geropsychiatric Rounds," Barry S. Fogel, MD, Director, Psychiatric Medical Program, Rhode Island Hospital, (401)464-3456.

17 General Hospital, Rhode Island Medical Center, "Clinico-Pathologic Conference," Speakers — Invited discussors and Pathology Staff, (401)464-3456.

30 Brown University Program in Medicine, "Violence in Adolescence," William Dietz, MD, Richard Gelles, PhD, Joseph Greensher, MD, Eva Deykin, PhD, Nancy Jander, RN, Sponsor — New England Chapter Society for Adolescent Medicine, (401)863-3337.

OCTOBER

13 General Hospital, Rhode Island Medical Center, "Geropsychiatric Rounds," Barry S. Fogel, MD, Director, Psychiatric Medical Program, Rhode Island Hospital, (401)464-3456.

15 General Hospital, Rhode Island Medical Center, "Clinico-Pathologic Conference," Speakers — invited discussors and Pathology Staff, (401)464-3456.

22-24 Brown University, "Mental Images," Speakers — more than 20 speakers involved in college health, Sponsor — Brown University Health Services, New England Health Association, (401)863-3337.

26 General Hospital, Rhode Island Medical Center, Topics on the Central Nervous System (series), Stanley M. Aronson, MD, University Professor of Medical Science, Brown University Medical Program, (401)464-3456.

31 Brown University Program in Medicine, "Therapies for Acute Myocardial Infarction: 1987," Marc A. Pfeffer, MD, PhD, William E. Boden, MD, Richard A. Carleton, MD, Abdul H. Khan, MD, Kenneth Korr, MD, David Williams, MD, Robert Capone, MD, (401)863-3337.

NOVEMBER

9 General Hospital, Rhode Island Medical Center, Topics on the Central Nervous System (series), Stanley M. Aronson, MD, University Professor of Medical Science, Brown University Medical Program, (401)464-3456.

17 General Hospital, Rhode Island Medical Center, "Geropsychiatric Rounds," Barry S. Fogel, MD, Director, Psychiatric Medical Program, Rhode Island Hospital, (401)464-3456.

19 General Hospital, Rhode Island Medical Center, "Clinico-Pathologic Conference," Speakers — invited discussors and Pathology Staff, (401)464-3456.

DECEMBER

2 Brown University Program in Medicine, "An Oncology Update for Practicing Physicians," Speakers to be announced, Sponsor — Roger Williams General Hospital, (401)863-3337.

14 General Hospital, Rhode Island Medical Center, Topics on the Central Nervous System (series), Stanley M. Aronson, MD, University Professor of Medical Science, Brown University Medical Program, (401)464-3456.

22 General Hospital, Rhode Island Medical Center, "Geropsychiatric Rounds," Barry S. Fogel, MD, Director, Psychiatric Medical Program, Rhode Island Hospital, (401)464-3456.

CONTINUING SERIES

General Hospital, Rhode Island Medical Center (464-3456)

Twice Monthly (TBA)		AIDS — Clinical Rounds Charles C.J. Carpenter, MD, Chief of Medical Service, The Miriam Hospital, Professor of Medicine, Brown University Program in Medicine.

Woman & Infants Hospital

Tuesday	7:30 am	Obstetrics and Gynecology Tumor Board Meeting (call for agenda — 274-1100, ext. 1588)
Wednesday	7:45 am	Perinatal Management Conference Call for speakers and subject matter (274-1100, ext. 1584)
Saturday	8:00 am	Grand Rounds Team Chief and Chief Resident OB/GYN (274-1100, ext. 1579, 1584)
Saturday	9:00 am	Guest Lecturer Call Dept. of Medical Education for speaker and subject matter (274-1100, ext. 1579, 1584)

Children and the Space Shuttle Tragedy

A Strategy Should be Developed for Dealing With Traumatic National Events

Shawn Cooper, PhD, MPH

On January 28, 1986, the Space Shuttle Challenger was destroyed shortly after liftoff, resulting in the loss of the seven astronauts aboard. Great concern was expressed in the media regarding the potential adverse effect this tragedy might have on children, since one of the astronauts was a teacher and because many children had witnessed the event on television at their schools.

Method

Assuming that parents who were concerned about their child's reaction to this event would contact the child's physician, the present author composed a letter to physicians which briefly described the event, possible child reactions, and several strategies for the physician to use in responding to parental concerns.

Within one week after the event, this letter and a stamped return envelope was sent to essentially all the pediatricians and family practitioners listed in the 1985 Rhode Island Medical Society Directory. A total of approximately 75 letters was sent.

The letter also contained a tearoff portion which physicians were requested to return at the end of February, one month after the event. The tearoff section contained several questions regarding the physician, as well as several questions regarding the number and type of calls which had been received regarding the shuttle tragedy during the month and whether the physician had referred any children for further mental health services.

At the end of February 1986, the author consulted the Providence, Rhode Island Telephone Yellow Pages and located the seven child psychiatrists listed. A letter was sent to these psychiatrists, explaining the nature of the present survey and asking if they had had any referrals within the past month which were directly, or indirectly, related to the shuttle accident; and whether or not any of their patients who were in treatment at the time of the accident showed any significant reaction to the event.

Results

Over the several weeks after the letters to pediatricians and family physicians were mailed, a total of ten responses were received, nine using the form and one by phone (one additional response was received some months later). Of the total of eleven physician responses, nine indicated that they had received no calls from parents regarding child reactions to the tragedy. One physician indicated having received under 25 calls (the smallest response category on the questionnaire), including children from six through 18, all with anxiety symptoms, and he had referred none for further mental health services. The other physician who indicated receiving any calls had received two, one from a family where the child had had two deaths in her own family in the past year, one of which had occurred in the week

Shawn Cooper is a clinical psychologist in private practice in Providence, Rhode Island, specializing in consultation, assessment, and treatment of children, adolescents and families.

before the shuttle accident. This physician had referred one patient for further mental health services.

Of the seven psychiatrists who had been contacted, four responded. None of them had gotten any referrals related to the accident, nor did any of them report a significant reaction among patients already in treatment.

Discussion

Several observations may be made about this survey effort. First, a small number of physicians (only 13 to 14 per cent) responded to the questionnaire. Second, it appeared that few physicians actually received calls reflecting children's reactions to the shuttle tragedy. There was some evidence suggesting that where children did show a reaction it was because the shuttle accident occurred at a time when the child was dealing with other losses.

The results of the survey of psychiatrists suggests that few children who did react to the shuttle tragedy had found their way to private psychiatrists within the month following the event and those children already in therapy did not show a significant reaction to the tragedy.

The findings of this survey effort raise several issues. First, it is possible that other approaches (eg, sending a survey letter near the end of February and asking for an immediate reply) would have resulted in a higher physician response rate. However, if one assumes that the responses which were obtained accurately reflected the general experience of physicians in Rhode Island, other conclusions are possible. They include the following: children in Rhode Island were not significantly distressed by the event; children did respond significantly, but were assisted by in-school programs that were established; or school programs were set up so quickly that they prevented children from reacting and appearing in the physician system.

Whichever of the above views may be valid the survey implies that the medical community, particularly that part of it which deals with children, may need to develop a general strategy for responding to adverse reactions to traumatic national events, however rare they may be.

170 Waterman Street
Providence, Rhode Island 02906

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

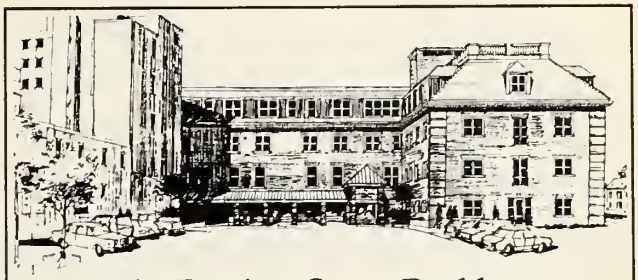
HAVE YOU HEARD? . . .

In a recent issue of *Cardiology Mgt.* a new thrombolytic agent called tissue plasminogen activator (t-PA) that dissolves blood clots may prove effective in reducing damage and death due to heart attack, according to Burton Sobel, MD, professor of medicine and director of the cardiovascular division at Washington University School of Medicine at St. Louis. When injected directly into the coronary blood vessels of several thousand patients, t-PA dissolved obstructing clots in 70-75 per cent of cases within one hour of the start of heart attack symptoms.

Dr. Sobel sees the possibility in the future of routine t-PA intravenous injection at the first sign of a heart attack. He cautions, however, that perfecting such an injection will require in-depth research, tight controls, close medical observation, and well-educated patients. At present, it takes three to six hours to take effect when administered intravenously. Scientists are presently researching absorption-enhancement agents to increase delivery of the substance to the heart vessels through intramuscular injection. Testing is also being done to reduce the risk of bleeding complications that may result when t-PA interacts with heparin. A further complication following dissolution of the clot is the surge of blood back into oxygen-starved heart muscle, which can damage heart tissues. The use of calcium blockers along with t-PA in order to lessen some of the damaging effects is under investigation.

• • •

The Food and Drug Administration has given approval for marketing in the United States of the first implantable electrical bone-growth stimulator for the spine. Osteostim HS11 increases the success rate of spinal fusions from 54 per cent to 81 per cent in a prospectively randomized controlled clinical study. BGS Medical is the company responsible for developing the new device. Only difficult cases (defined as previous failed fusions, grade II or worse spondylolisthesis multiple level fusion requiring extensive grafting, or patients at increased risk for failure due to age, obesity, disease, debility, or metabolic disorder) were the subjects for the clinical trials, which made



The Borden-Carey Building
Medical and Office Condominiums

NOW AVAILABLE FOR SALE
OR LEASE

Conveniently located at 19 Friendship St.,
Adjoining Newport Hospital

Individual Suites are now available for
interior design and tenant finish.

Priced to sell from $80,000 and to
lease for $15.00/s.f.

For further information call:

RE
Ryan Elliott

Ryan Elliott & Co. of Rhode Island, Inc.
401-331-0350

BANNISTER NURSING
CARE CENTER

A non-profit facility established in 1890

Immediate openings have been created to expand our medical staff. Qualified physicians are invited to visit our facility and join our team. Your inquiry should be directed to:

Mr. Richard E. Miller
Administrator
135 Dodge Street
Providence, Rhode Island 02907
401/274-3220

the results more significant, according to Christopher Roberts, PhD president of BGS Medical.

Along with this randomized clinical study involving 99 patients, the FDA looked at data from a non-randomized study of 116 patients which produced a 93 per cent fusion success. Earlier study results were also presented involving 82 patients treated with the Osteostim HS11 over a 12-month period. This resulted in 92 per cent successful fusions in comparison with another control study in which 128 of 159 patients, or 81 per cent, achieved success.

The Osteostim HS11 is indicated as an adjunct to spinal fusion to promote successful fusion at one or more levels. A constant direct electrical current is applied to induce bone growth. Four cathodes are implanted during spinal surgery directly into the bone, while a generator is positioned in the soft tissue about 8 centimeters from the cathodes. The Osteostim HS11 system is left in this position for approximately 26 weeks, after which time it is removed by the surgeon under local anesthesia on an outpatient basis.

• • •

Wearing running shoes could reduce foot problems or possible foot amputations of persons with diabetes, this from an 18-month study reported in the Spring 1987 issue of *The Diabetes Educator.* The study, supported by a grant from the Centers for Disease Control and funded through the Utah Diabetes Control Program, focused on 100 diabetic volunteers with plantar calluses. Many diabetes-related amputations are the result of ulcerated, infected, and gangrenous plantar calluses.

Author Scott M. Soulier, DPM, MSPH, a podiatric consultant at the Utah Diabetes Control Program in Salt Lake City, in the *Report of the National Commission on Diabetes* estimates that 5 to 15 per cent of persons with diabetes will suffer a lower-extremity amputation in their lifetime. The considerable hospital costs resulting from 17,000-20,000 lower extremity amputations each year in the US can be reduced. Foot problems are often caused by abnormal pressure or friction on the plantar surface of the foot and can be corrected by proper footwear. Running shoes are more appropriate for diabetics because of their specific cushion design as compared to regular shoes. Informational literature on diabetic foot care should include advice on wearing well-cushioned and padded footwear. Cynthia Godsey, RN, MS, director, and Elvin D. Asay, MS, statistician at the Utah Diabetes Control Program, and Dennis M. Perrotta, PhD, epidemiologist, Bureau of Epidemiology at the Utah Department of Health participated in the study.

• • •

Parents of pediatric patients seem to feel that a doctor's attire influences perception of his/her competence, according to a report in the April 1987 issue of *American Journal of Diseases of Children.* The study by Paul G. Taylor, MB, MRCP (UK), FRCPC, DCH, of the University of Alberta, Edmonton, Canada, used a random sample of parents of pediatric inpatients at a university teaching hospital. Using sets of photographs of house staff physicians wearing different outfits, he found that a doctor in formal dress (formal street clothes and long white laboratory coat) was twice as likely to be labeled competent as one in operating room clothing (surgical greens, short laboratory coat, casual shoes). The formal dress rating was four times as likely to be labeled competent as compared to physicians wearing an intern uniform (casual pants and shoes, short laboratory coat). Those parents with a university education and those who had never had a child hospitalized were less likely to make these assumptions. The study reports that the doctor's gender has no effect on perceptions of competence.

• • •

American College of Physicians (ACP) has issued recommendations for treating rheumatoid arthritis (RA) with methotrexate, a folic acid antagonist and anti-cancer drug. Methotrexate, although not yet approved by the US Food and Drug Administration (FDA) for this purpose, has become the second or third choice drug for treating the 2.1 million Americans afflicated with established rheumatoid arthritis.

The recommendations were developed by ACP's Clinical Efficacy Assessment Project (CEAP) based on analysis of four placebo-controlled clinical trials documenting the short-term clinical benefits of methotrexate. Patients can expect a partial reduction in the number of painful, inflamed joints as well as reduction in overall pain, although according to present data true remission is rare. The CEAP recommends that methotrexate (given orally or intramuscularly), can be used if both first-and second-line agents for RA as well as injectable gold and d-penicillamine have not been successful. A list of absolute and relative contraindications and a suggested dosage and monitoring schedule are provided.

Rhode Island

ADVERSE DRUG REACTION Reporting Project

SUSPECT A SERIOUS OR UNEXPECTED

ADVERSE DRUG REACTION?

Please Report It.

SUSPECTED ADVERSE REACTION REPORT (For All Drugs and Biologics)

IMPORTANT: SUBMISSION OF A REPORT DOES NOT NECESSARILY CONSTITUTE AN ADMISSION THAT THE DRUG CAUSED THE ADVERSE REACTION

PATIENT INITIALS (Optional)	AGE (Years)	SEX	DATE OF REACTION ONSET
A.D.R.	54	[/] MALE [ ] FEMALE	12 Oct. 1986

DESCRIBE REACTION(S) (Give signs, symptoms, diagnoses, course and lab findings)

JAUNDICE

CHECK ALL APPROPRIATE TO REACTION
- [ ] DIED
- [/] TREATED WITH Rx DRUG
- [/] INPATIENT HOSPITALIZATION
- [ ] SEVERE OR PERMANENT DISABILITY
- [ ] EMERGENCY ROOM TREATMENT
- [ ] TREATMENT IN PHYSICIAN OFFICE
- [ ] NONE OF THE ABOVE

SUSPECTED DRUG(S) (Trade Name is preferred. If a generic product, give manufacturer. Indicate Lot No. for vaccines, biologics)

[redacted]

REASON FOR USE OF DRUG(S)	ROUTE	TOTAL DAILY DOSE	DATES OF ADMINISTRATION
HYPERTENSION	P.O.	100mg.	9 Sept.- 12 Oct. '86

OTHER DRUGS TAKEN CONCOMITANTLY (Exclude those used to treat reaction)

None

OTHER RELEVANT HISTORY (e.g., Concomitant Diagnoses, Pregnancy, etc.)

None

PHYSICIAN NAME AND TELEPHONE NUMBER

J. Doe, M.D. 277-2550

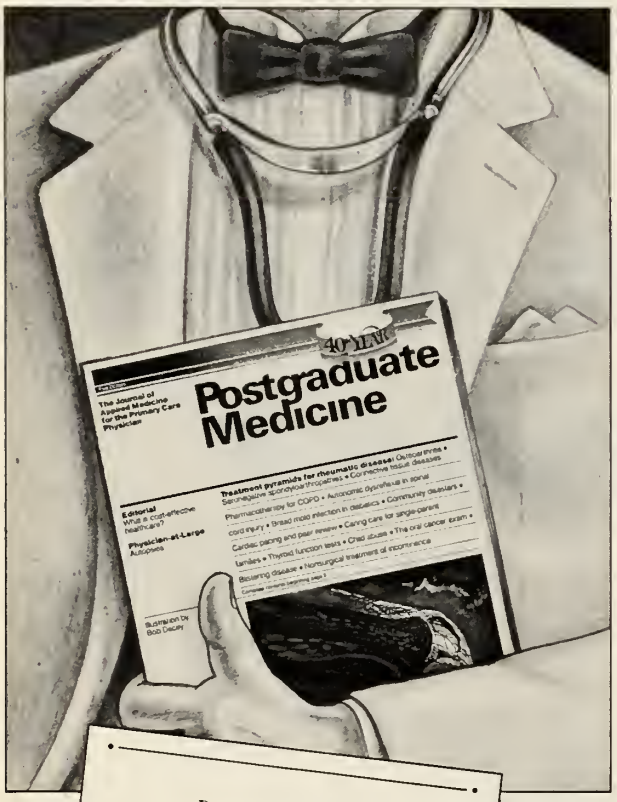
Confidential

ALSO REPORTED TO MANUFACTURER [/] YES [ ] NO

For report forms, guidelines and information contact S. Rosenbaum, PhD, 277-2901

A pilot project of the Rhode Island Department of Health
sponsored by the U.S. Food and Drug Administration

FAMOUS PHYSICIANS ARE SHOWING UP FOR OUR 40th YEAR CELEBRATION.



Paul P. Griffin, M.D.
Robert G. Petersdorf, M.D.
Eric A. Ravitz, D.O.
J. Jerry Rodos, D.O.
Professor H.E. de Wardener, C.B.E.

Read Every Issue From Cover to Cover:

July
Symposium: Skeletal Problems
Special Article: Orthopedics 1947-1987 . . . . . Paul P. Griffin, M.D.

August
Symposium: Infectious Diseases
Special Article: Infectious Diseases 1947-1987 . . Robert G. Petersdorf, M.D.

September 1
Symposium: Focus on Osteopathic Medicine . . . . . Eric A. Ravitz, D.O. Coordinator
Special Article: Osteopathic Medicine 1947-1987 . . . J. Jerry Rodos, D.O.

September 15
Symposium: Renal Disease
Special Article: Renal Disease 1947-1987 . . . . Professor H.E. de Wardener, C.B.E.

40th YEAR
Postgraduate Medicine

Every Issue is a Celebration of Clinical Information

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

MEDICAL OFFICE SUITE

IN MODERN, LUXURIOUS MEDICAL COMPLEX

2000 SQUARE FEET

LEASE NEGOTIABLE

WILL DIVIDE FOR SUITABLE TENANTS

WELL TRAVELED, CENTRALLY LOCATED AREA WITH EASY ACCESS

For further details
Call D. Merola
353-6362
9 am - 3 pm, Mon. - Fri.

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

Employment Opportunity

FAMILY PRACTICE PHYSICIANS

are needed for private, non-profit community health centers with growing practices in Rhode Island.

Applicants must be board-eligible or certified. Positions are open in suburban and urban centers, full or part time. Competitive compensation package including pro-rated malpractice insurance and continuing medical education benefits.

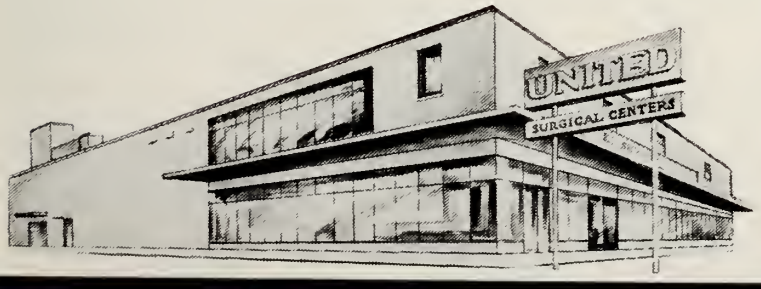
Send curriculum vitae to:

Resources Coordinator
RHODE ISLAND HEALTH CENTER ASSOCIATION
2845 Post Road, Rm. 110
Warwick, RI 02886
(401) 732-3778

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

We've Reduced the Rates on Our 5 Year Renewable Group Term Life Insurance

Take Advantage of Your Group Purchasing Power

$100,000.00

Non-Smoker Rates

ANNUAL COST

AGE	MALE OLD	MALE NEW (NON SMOKER PREMIUM)	FEMALE OLD	FEMALE NEW (NON SMOKER PREMIUM)
Under 30	$ 107.00	$ 79.00	$ 86.00	$ 63.00
30–34	$ 119.00	$ 81.00	$ 94.00	$ 65.00
35–39	$ 169.00	$116.00	$116.00	$ 87.00
40–44	$ 299.00	$185.00	$202.00	$147.00
45–49	$ 515.00	$319.00	$346.00	$241.00
50–54	$ 861.00	$510.00	$576.00	$380.00
55–59	$1,293.00	$859.00	$864.00	$627.00

1) Maximum Benefit available for member $300,000.00
2) Full Benefit to Age 70
3) Conversion Benefit Without Medical Evidence to a Permanent Life Plan
4) Waiver of Premium Benefit Included
5) No Physical Examination Required
6) Coverage for Spouse up to $150,000

Endorsed by the
RHODE ISLAND MEDICAL SOCIETY

The Administrators
LB personal service since 1922
LESTER L. BURDICK, INC.
Loyalty Group Insurance
10 POST OFFICE SQUARE, BOSTON, MA 02109
(617) 426-0020

Underwritten by: COMMERCIAL INSURANCE COMPANY 15 Corporate Place South, Piscataway, NJ 08854. 201/981-4842

Motrin® 800 TABLETS mg

ibuprofen

Extra strength
Convenience
Economy

Upjohn

A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

News from DISTA about a new dosage form of cephalexin

ANNOUNCING NEW

Keflet™
TABLETS
cephalexin

All the advantages of cephalexin in a convenient tablet form

- Backed by over 15 years of clinical experience
- Smaller tablet is specially shaped and coated for easier swallowing
- May enhance patient compliance, particularly among the elderly
- Tablet dosage form may be appreciated by patients of all ages

NEW Keflet Tablets are available as:

250-mg Tablets

500-mg Tablets

Keflet is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-sensitive patients.

© 1987 DISTA PRODUCTS COMPANY

Brief Summary. Consult the package literature for prescribing information.
Indications and Usage: Keflet™ Tablets (cephalexin, Dista) are indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Respiratory tract infections caused by *Streptococcus pneumoniae* and group A β hemolytic streptococci (Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Keflet is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of Keflet in the subsequent prevention of rheumatic fever are not available at present.)

Otitis media due to *S pneumoniae, Haemophilus influenzae*, staphylococci, streptococci, and *Neisseria catarrhalis*

Skin and skin-structure infections caused by staphylococci and/or streptococci

Bone infections caused by staphylococci and/or *Proteus mirabilis*

Genitourinary tract infections, including acute prostatitis, caused by *Escherichia coli, P mirabilis*, and *Klebsiella* sp

Note—Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

Contraindication: Keflet is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: BEFORE CEPHALEXIN THERAPY IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS AND PENICILLIN. CEPHALOSPORIN DERIVATIVES SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS.

SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and the cephalosporins. Patients have been reported to have had severe reactions (including anaphylaxis) to both drugs.

Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics cautiously. No exception should be made with regard to Keflet.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins), therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C difficile*. Other causes of colitis should be ruled out.

Usage in Pregnancy—Safety of this product for use during pregnancy has not been established.

Precautions: *General*—Patients should be followed carefully so that any side effects or unusual manifestations of drug idiosyncrasy may be detected. If an allergic reaction to Keflet occurs, the drug should be discontinued and the patient treated with the usual agents (eg, epinephrine or other pressor amines, antihistamines, or corticosteroids).

Prolonged use of Keflet may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Keflet should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

As a result of administration of Keflet, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy—Pregnancy Category B—The daily oral administration of cephalexin to rats in doses of 250 or 500 mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, fetal viability, fetal weight, or litter size. Note that the safety of cephalexin during pregnancy in humans has not been established.

Cephalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals. Nevertheless, because the studies in humans cannot rule out the possibility of harm, Keflet should be used during pregnancy only if clearly needed.

Nursing Mothers—The excretion of cephalexin in the milk increased up to 4 hours after a 500-mg dose, the drug reached a maximum level of 4 μg/mL, then decreased gradually, and had disappeared 8 hours after administration. Caution should be exercised when Keflet is administered to a nursing woman.

Adverse Reactions: *Gastrointestinal*—Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely. The most frequent side effect has been diarrhea. It was very rarely severe enough to warrant cessation of therapy. Dyspepsia and abdominal pain have also occurred. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity—Allergic reactions in the form of rash, urticaria, angioedema, and, rarely, erythema multiforme, Stevens-Johnson Syndrome, or toxic epidermal necrolysis have been observed. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported.

Other reactions have included genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue, and headache. Eosinophilia, neutropenia, thrombocytopenia, and slight elevations in SGDT and SGPT have been reported.

PV 2211 DPP [111786]

Additional information available to the profession on request from

DISTA

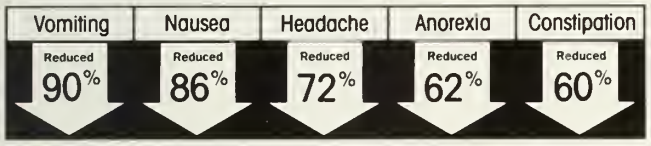
Dista Products Company
Division of Eli Lilly and Company
Indianapolis, Indiana 46285
Mfd by Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

720073

See the difference in the first week[1]

- **Sleep improvement in 74% of patients after first h.s. dose[2]**
- **Significantly faster relief–62% of total four-week improvement evident in first week versus 44% with amitriptyline alone[1]**
- **Dramatic first-week reduction in somatic complaints[2]**

% Reduction in Somatic Symptoms[2]



- **Only ⅓ the dropout rate due to side effects of amitriptyline alone, although the incidence of side effects is similar[1]**

Cautian patients abaut the cambined effects af Limbitral with olcohol ar other CNS depressants and about activities requiring complete mental olertness, such as aperating mochinery ar driving a car. In general, limit dosage ta the lawest effective amount in elderly patients.

Protect your decision.
Write "Do not substitute."

In moderate depression and anxiety

Limbitrol®

Eoch toblet contoins 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochlaride solt) (IV)

Limbitrol® DS

Eoch tablet contoins 10 mg chlordiazepoxide ond 25 mg omitriptyline (as the hydrochloride solt) (IV)

Copyright © 1987 by Roche Products Inc. All rights reserved.

References: 1. Feighner JP, *et al. Psychopharmacology 61* 217-225, Mar 22, 1979 **2.** Data on file, Hoffmann-La Roche Inc , Nutley, NJ

Limbitrol® (IV)
Tranquilizer—Antidepressant
Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of moderate to severe depression associated with moderate to severe anxiety
Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use, then initiate cautiously, gradually increasing dosage until optimal response is achieved Contraindicated during acute recovery phase following myocardial infarction.
Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs Closely supervise cardiovascular patients (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses Myocardial infarction and stroke reported with use of this class of drugs) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving)

***Usage in Pregnancy*: Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage, withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline, symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide)
Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients Periodic liver function tests and blood counts are recommended during prolonged treatment Amitriptyline component may block action of guanethidine or similar antihypertensives When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated, sedative effects may be additive Discontinue several days before surgery Limit concomitant administration of ECT to essential treatment See Warnings for precautions about pregnancy Limbitrol should not be taken during the nursing period Not recommended in children under 12 In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects
Adverse Reactions: Most frequently reported are those associated with either component alone drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely
The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs
Cardiovascular Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke
Psychiatric Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libida
Neurologic Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns
Anticholinergic Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract
Allergic Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus
Hematologic Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia
Gastrointestinal Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue
Endocrine Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion
Other Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling
Overdosage: Immediately hospitalize patient suspected of having taken an overdose Treatment is symptomatic and supportive IV administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning See complete product information for manifestation and treatment
Dosage: Individualize according to symptom severity and patient response Reduce to smallest effective dosage when satisfactory response is obtained Larger portion of daily dose may be taken at bedtime Single *h.s.* dose may suffice for some patients Lower dosages are recommended for the elderly Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses
How Supplied: *Double strength (DS) Tablets*, white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets*, blue, film-coated, each containing 5 mg chlordiazepoxide and 12 5 mg amitriptyline (as the hydrochloride salt) Available in bottles of 100 and 500, Tel-E-Dose® packages of 100, Prescription Paks of 50

ROCHE®
ROCHE PRODUCTS INC
Manati, Puerto Rico 00701

PI 0585

The rewards of Limbitrol
You're both smiling agai

EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

See the difference in the first week[1]

In depressed and anxious patients, you can see the difference sooner—62% of total four-week improvement achieved in the first week with Limbitrol versus 44% with amitriptyline.[1]

In moderate depression and anxiety

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) (IV)

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) (IV)

ROCHE®

Please see summary of product information on adjacent page.

Rhode Island Medical Journal

August 1987
Volume 70, Number 8

Doctor and Mrs. Herbert Rakatansky (RIMS Past President), Doctor and Mrs. Richard G. Bertini (RIMS President), Doctor William S. Hotchkiss (AMA President), and Doctor and Mrs. Peter D. T. Clarisse (RIMS Immediate Past President)

CONTRIBUTIONS

341 Certificate of Need: A State Perspective

347 Diagnosis, Significance, and Treatment of Neonatal Seizures

355 Presidential Address

361 Cautions to Young Persons Concerning Health

339 EDITORIAL

375 PERIPATETICS

377 HAVE YOU HEARD?

381 BOOKS RECEIVED

SAVE THIS DATE

SIXTH ANNUAL ELLA T. GRASSO MEMORIAL CONFERENCE
November 18, 1987

This symposium addresses current clincial problems in gynecologic oncology and research developments that will impact on patient care. It is directed toward obstetricians/gynecologists, medical oncologists, radiation therapists, pathologists, nurses and residents. The symposium is sponsored by the Divisions of Gynecologic Oncology at the Yale University School of Medicine, the Yale Comprehensive Cancer Center and the University of Connecticut School of Medicine.

Location

The Park Plaza
155 Temple Street
New Haven, CT 06511
(203) 772-1700

Guest Faculty

J. Taylor Wharton, M.D.
M. D. Anderson Hospital and Tumor Institute

Peter Wiernik, M.D.
Montefiore Hospital Medical Care

Richard I. Reid, M.D.
Sinai Hospital of Detroit

Howard W. Jones, III, M.D.
Vanderbilt University Medical Center

Maria Merino, M.D.
NIH — NCI

Jeffrey Schlom, M.D.
NIH — NCI

For registration and further information (after AUGUST 1, 1987):

Yale University School of Medicine
Office of Graduate and Continuing Education
New Haven, CT 06510
(203) 785-4578

Motrin® 800 TABLETS mg

ibuprofen

Extra strength
Convenience
Economy

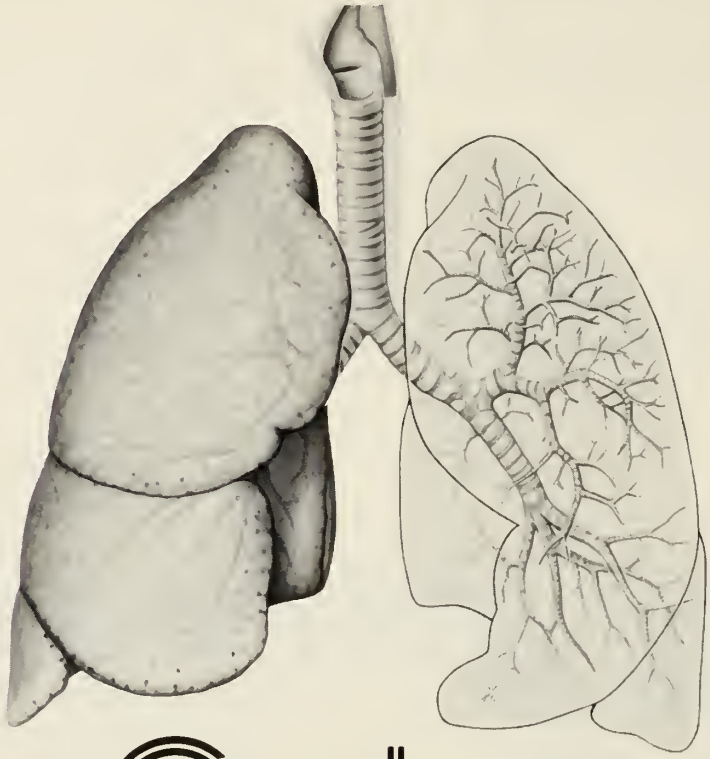
Upjohn

A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, Streptococcus pneumoniae
(ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Contraindication:
Known allergy to cephalosporins.

Warnings:
CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly).

[072886R]

PA 8794 AMP

©1987, ELI LILLY AND COMPANY

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

700241

Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were treated merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA.

The one you know best keeps looking better

NOW AVAILABLE...
NEW LOW DOSE
INDERAL LA 60 mg
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. INDERAL LA is formulated to provide a sustained release of propranolol hydrochloride. INDERAL LA is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective, beta-adrenergic receptor-blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (60, 80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period, the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL Tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours, then decline exponentially.

INDERAL LA should not be considered a simple mg-for-mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension. It may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

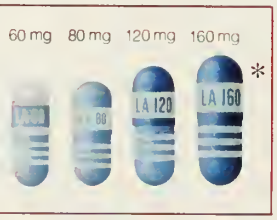
CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first-degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES



WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely; or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (eg, chronic bronchitis, emphysema). PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta blockers should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. Following insulin-induced hypoglycemia, propranolol may cause a delay in the recovery of blood glucose to normal levels.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol may change thyroid function tests, increasing T_4 and reverse T_3, and decreasing T_3.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. GENERAL. Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

CLINICAL LABORATORY TESTS. Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Caution should be exercised when patients receiving a beta blocker are administered a calcium-channel-blocking drug, especially intravenous verapamil, for both agents may depress myocardial contractility or atrioventricular conduction. On rare occasions, the concomitant intravenous use of a beta blocker and verapamil has resulted in serious adverse reactions, especially in patients with severe cardiomyopathy, congestive heart failure or recent myocardial infarction.

Aluminum hydroxide gel greatly reduces intestinal absorption of propranolol.

Ethanol slows the rate of absorption of propranolol.

Phenytoin, phenobarbitone, and *rifampin* accelerate propranolol clearance.

Chlorpromazine, when used concomitantly with propranolol, results in increased plasma levels of both drugs.

Antipyrine and *lidocaine* have reduced clearance when used concomitantly with propranolol.

Thyroxine may result in a lower than expected T_3 concentration when used concomitantly with propranolol.

Cimetidine decreases the hepatic metabolism of propranolol, delaying elimination and increasing blood levels.

Theophylline clearance is reduced when used concomitantly with propranolol.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

PREGNANCY. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS. INDERAL is excreted in human milk. Caution should be exercised when INDERAL (propranolol HCl) is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. Bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. Light-headedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, vivid dreams, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics. For immediate formulations, fatigue, lethargy and vivid dreams appear dose related.

Gastrointestinal. Nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. Pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. Bronchospasm.

Hematologic. Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. Alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL Tablets to INDERAL LA Capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg-for-mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three- to seven-day intervals until optimal response is obtained. Although individual patients may respond at any dosage level, the average optimal dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimal migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximal dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985; 145:1321-1323.

1R7119/887

Ayerst AYERST LABORATORIES
New York, NY 10017

© 1987 Ayerst Laboratories

August 1987
Volume 70, Number 8

Rhode Island Medical Journal

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Edward R. Feller, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***Guy A. Settipane, MD**

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401 331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

The Trustees of the Fiske Fund of the Rhode Island Medical Society are pleased to announce the

FISKE PRIZE FOR 1987

to be awarded for an original contribution on

"AIDS Pandemic . . . Etiology, Incidence, Distribution, & Control"

The award is named after Caleb Fiske (1753-1834), who was a Rhode Island physician and judge, Army surgeon, and a descendent of Roger Williams. Since the prize was initiated in 1836, 87 awards have been made for original contributions. Previous recipients include Charles V. Chapin, Providence, internationally known for his research on public health; David King, Jr., Newport who received the award in 1836 for his paper on "Purpura Haemorrhagica: Its Causes and Treatment"; and Alton Oschner, New Orleans, who received the 1958 award for his paper entitled "Bronchogenic Carcinoma: Predisposing Causes."

The award for the 1987 Fiske Prize will be a maximum of $2,500. The Trustees reserve the right to award one or more prizes. The competition is not restricted to physicians.

Guidelines:

1) The original and one copy must be submitted by Aug. 24, 1987 to Secretary, Caleb Fiske Fund of the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903.
2) All papers must be double-spaced and should not exceed 10,000 words.
3) The award recipient must transfer copyright privileges to the Trustees of the Caleb Fiske Fund of the Rhode Island Medical Society. The paper will be considered for publication in the *Rhode Island Medical Journal*, subject to review by the Editorial Board.
4) The award recipient will also present his/her prize winning paper at a symposium to be scheduled in the Fall commemorating the 175th anniversary of the Rhode Island Medical Society.

Rhode Island Medical Journal Volume 70, Number 8 August 1987

TABLE OF CONTENTS

339 **EDITORIAL**

State Medical Journals

Seebert J. Goldowsky, MD

375 **PERIPATETICS**

377 **HAVE YOU HEARD?**

381 **BOOKS RECEIVED**

CONTRIBUTIONS

341 **Certificate of Need: A State Perspective**

This Is Not the Time to Discard Certificate of Need

H. Denman Scott, MD, MPH
John T. Tierney, MSW
William J. Waters, PhD
Donald C. Williams, MA
John X. Donahue, MPA

347 **Diagnosis, Significance, and Treatment of Neonatal Seizures**

Recommendations Are Made For An Approach To Suspected Seizures Based On Updated Information

Edwin L. Zalneraitis, MD

355 **Presidential Address**

Peter D. T. Clarisse, MD

361 **Cautions to Young Persons Concerning Health**

Shewing the Evil Tendency of the Use of Tobacco Upon Young Persons

Benjamin Waterhouse, MD

COVER: *The receiving line for the 175th Annual Dinner Dance of the Rhode Island Medical Society, held at Rosecliff Mansion, Newport, RI. Photographer — John Corbett.*

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue
Providence, R.I.
331-3996

120 Dudley Street
Providence, R.I.
331-3996

154 Waterman Street
Providence, R.I.
273-0450

38 Hamlet Avenue
Woonsocket, R.I.
766-4224

EDITORIAL

State Medical Journals

Having just returned from a meeting of the board of the State Medical Journal Advertising Bureau in Chicago and recalling a recent (September 1986) biennial state journal conference of the Bureau in Austin, Texas, this writer wondered whether our readers are aware of what transpires in this little world.

The Bureau embraces 30 journals, 29 state and one county (Chicago). There are in all 34 state journals plus the incomparable *New England Journal of Medicine* and *Massachusetts Medicine,* both of which are owned by the Massachusetts Medical Society. The Bureau solicits national advertising for its members, traditionally pharmaceutical advertising, but for the past year non-pharmaceutical advertising as well. This journal has averaged in recent months as many as 17 pages of national advertising which compares favorably with the New York and Illinois journals, among the largest in circulation.

The Bureau's biennial conferences provide an invaluable service for the state journals. They offer teaching conferences on all phases of state medical journal publishing — editing, graphics, content, appearance, and the secrets of attracting advertising. There is usually a professor of journalism on the program. This journal has profited greatly from regular attendance at these conferences.

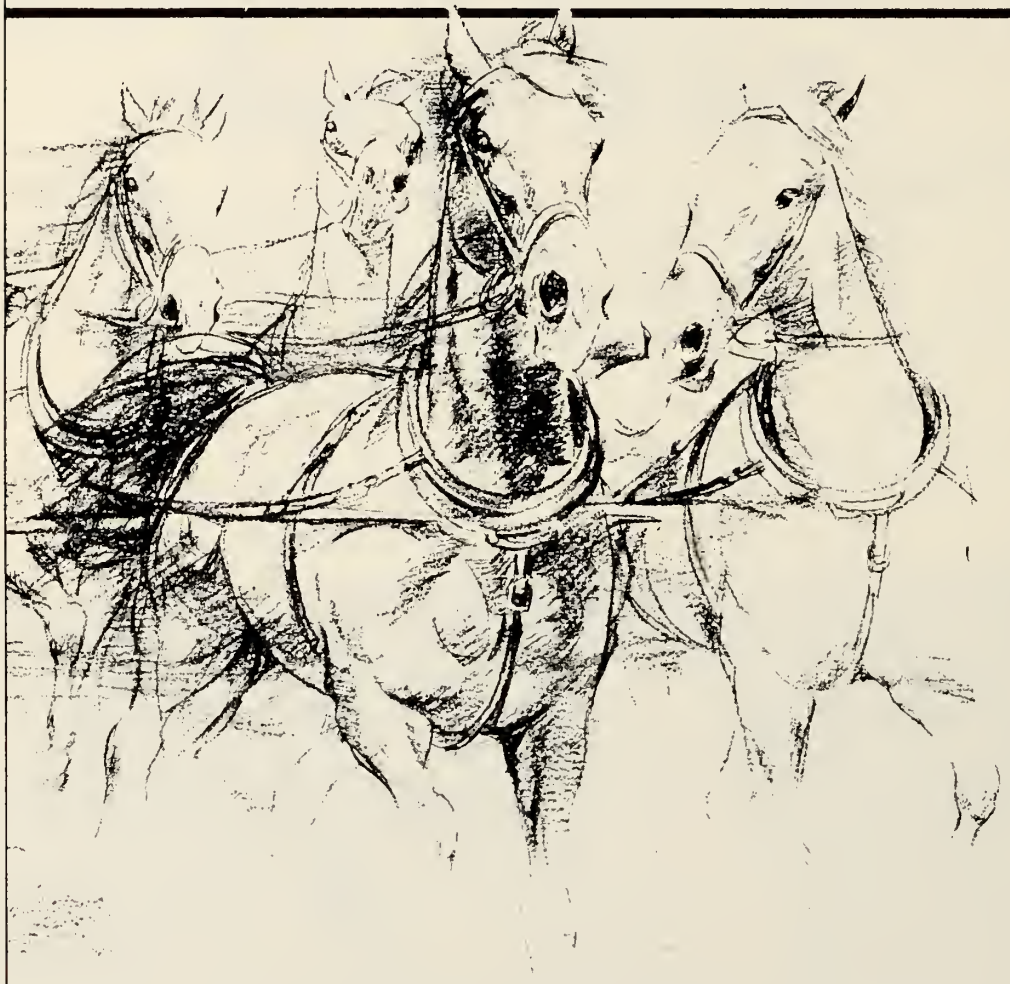
There is cynicism in some quarters as to the value and role of state journals. We have heard the sour comment on more than one occasion: "I never read it!" But this is far from universal. We regularly receive feedback from readers — favorable comment on editorials, reaction to papers, letters, and occasional brickbats.

A survey of nine state journals of various sizes by Health Industries Research produced some surprising results. The number of physicians who read an average issue came out at an astounding 78 per cent. The average issue ad exposure was even more surprising at 42 per cent compared to 12 to 15 per cent for *JAMA* and *Medical Economics.* When asked whether they wished to continue receiving their journals an incredible 91 per cent replied in the affirmative. The average reading time per issue was a respectable 31 minutes. Twenty-nine per cent of readers reported that they saved issues for future reference.

For the minority of our constituents who believe that state medical journals are dead, these facts, we hope, will convince them that the state journals are alive and well.

Seebert J. Goldowsky, MD

The True Test Of An Investment Management Team Is Its Ability To Pull Together, With Separate Strengths.



Today, managing your financial assets demands a concerted team effort. And the capacity to respond to changes in the economic climate, while still focusing on your individual goals.

The Hospital Trust Investment Management and Trust Group is uniquely qualified to provide this combination of strengths.

Indeed, you'd have to hire specialists in stocks, bonds, real estate, precious metals and international investments to rival the diversity we offer under one roof.

Discover how you can harness this strength to reach your financial goals. For a uniquely objective evaluation of your investment needs or more information, call Gary Gherardini, Vice President, at 278-8730.

Hospital Trust

a BANK OF BOSTON company

INVESTMENT MANAGEMENT AND TRUST GROUP

Certificate of Need: A State Perspective

This Is Not the Time to Discard Certificate of Need

H. Denman Scott, MD, MPH
John T. Tierney, MSW
William J. Waters, PhD
Donald C. Williams, MA
John X. Donahue, MPA

Certificate of Need: A State Perspective
In the June 1986 issue of the *Rhode Island Medical Journal* Dr Joseph Chazan evaluates certificate of need as a "concept whose time has passed." Conclusions aside, we believe this is a very appropriate time to reassess certificate of need in Rhode Island.[1] We welcome intense scrutiny of the program.

H. Denman Scott, MD, MPH, is Director of Health with the Rhode Island Department of Health, Providence, RI.

John T. Tierney, MSW, is Deputy Director of Health with the Rhode Island Department of Health, Providence, RI.

William J. Waters, PhD, is Assistant Director for Health Policy with the Rhode Island Department of Health, Providence, RI.

Donald C. Williams, MA, is Chief of Medical Care Standards with the Rhode Island Department of Health, Providence, RI.

John X. Donahue, MPA, is Supervising Health Planner with the Rhode Island Department of Health, Providence, RI.

Origins
In 1968 Rhode Island was the second state in the nation to enact certificate-of-need (CON) legislation. Rhode Island's CON legislation was a direct result of the work of the Legislative Commission to Investigate Hospital Room Rates and to Study the Advisability of Placing Such Rates under State Regulation, which was chaired by Representative Anthony J. Brosco.[2] Rapidly rising hospital room rates and widespread consumer co-payments approaching 50 per cent for hospital services provided the stimuli for this legislative initiative. In 1967, the semi-private room charge in Rhode Island hospitals ranged from $23.20 to $43.79. For the 42 per cent of Blue Cross subscribers who were covered by indemnity-type policies, 34-46 per cent of these charges were personal out-of-pocket expenses.

However, the Brosco Commission was not prepared to recommend hospital rate setting in 1967. They saw certificate-of-need as a "first step to deal with the myriad of problems — both current and future — in bringing the best in health care to Rhode Island residents at the least possible cost."[3] They recommended that "The Council (Health Services Council) should pass on all proposals for establishment, expansion, or substantial modification of hospitals which should be made uniformly subject to approval of the Director of Health after receiving the advice of the Council."[4] The purpose of CON is to determine the need for proposed health service developments through a public review process.

Originally CON applied almost exclusively to hospitals. In 1974, the CON law was amended to add nursing homes. Practically all other health facilities were added to the CON law with the amendments of 1978. Today, Rhode Island has

one of the most comprehensive CON statutes in the country.

In 1975, all states were required to establish CON programs under Public Law 93-641, the National Health Planning & Resources Development Act. This national law was recently repealed in November 1986; but, nevertheless, forty-one states have maintained CON.[5] Furthermore, a number of the states which have eliminated state-legislated CON have retained the federal 1122 CON program, or imposed legislated health care construction moratoria or both.[6]

Contributions

CON should deter unneeded health facility developments. The fact that health facility proposals are openly examined from a public interest perspective in the CON process acts as an important check. This sentinel effect is very hard to measure, but it is probably CON's major contribution. Keeping in mind that the public sector is the source of about 40 per cent of personal health expenditures and over 50 per cent of institutional health expenditures, such oversight is justified.

It appears that CON in Rhode Island has fulfilled, at least in part, the original intent of the Brosco Commission. To some extent, CON has prevented the unnecessary duplication of expensive capital expenditures. This is reflected in the fact that roughly 33 per cent of the capital costs of CON applications acted upon during the period 1971-1986 were not accepted, withdrawn, modified, or denied (See Table 1). This is also reflected in the fact that Rhode Island has a relatively modest hospital bed supply — 3.7 acute-care community-hospital beds per 1,000 population (vs) 4.4 for the United States.[7]

CON was designed to act as a brake on the inherently inflationary incentives imbedded in the traditional fee-for-service, cost-reimbursement, health-insurance system. Under the historically dominant fee-for-service reimbursement system, the more services that were provided, the more revenue was generated. Thus, CON serves as a form of external economic discipline for systems where there are few internal incentives for such discipline.

CON promotes quality assurance by assessing the service volume and organizational scale of proposed projects. There is growing evidence of a direct relationship between the quantity of medical services provided and the health-status outcomes of the patients, especially with respect to surgical services.[8-10] CON often contributes to quality of care by reviewing expected volume of service or procedures.

CON promotes access to health care for indigent groups by assessing the impact of geographic locations/relocations and Medicaid participation by providers. Rhode Island CON reviews routinely examine the applicant's policies regarding the care of Medicaid beneficiaries and uninsured individuals.

CON moderates unhealthy competition in the health sector. While competition between Health Maintenance Organizations (HMOs) may have a salutary effect on health-care costs, it has been demonstrated that competition between hospitals tends to increase hospital costs.[11] Hospitals usually compete with each other by adding expensive facilities, personnel, and technology. These enhancements, taken as whole, serve to exacerbate the health-care cost problem. CON acts as a counterforce to this uneconomical form of competition.

Table 1. Certificate of Need Program Performance 1971-1986

	Costs in Millions of Dollars					
	Capital Costs			Annual Operating Costs		
Description	Hospitals	Nursing Homes & Others	Total	Hospitals	Nursing Homes & Others	Total
1. All projects reviewed	342.8	210.8	553.6	68.5	117.5	186.0
2. Projects not accepted	4.6	39.8	44.4	2.9	19.7	22.6
3. Projects withdrawn	30.7	33.4	64.1	6.9	15.0	21.9
4. Modified projects	20.5	9.2	29.7	6.8	5.1	11.9
5. Projects denied	12.3	23.4	35.7	9.2	15.3	24.5
6. Projects approved	274.7	72.1	346.8	42.7	37.4	80.1
7. Projects pending	0.0	32.9	32.9	0.0	25.1	25.1
8. Total direct dollar savings (3)+(4)+(5)	63.5	66.0	129.5	22.9	35.4	58.3
9. Total dollar savings (2)+(3)+(4)+(5)	68.1	105.8	173.9	25.8	55.1	80.9

CON minimizes or prevents market-generated failures, closures, and dislocations. That is, CON facilitates a stable and fairly predictable environment for the management of health facilities. This allows health facility managers to concentrate on internal quality and efficiency concerns.

CON brings issues to the forefront which require systemwide study. For example, CON reviews in Rhode Island have stimulated systemwide planning for alcohol- and drug-abuse services, digital-subtraction angiography (DSA), nursing-home beds, and cardiac care.

The Rhode Island CON program requires providers to file annual institutional short-and long-range plans. Prior identification of a project in the institutional plan is a prerequisite for acceptance of a CON application. Thus, CON helps to stimulate sound institutional planning.

In summary, while CON is certainly no panacea for the health-care cost crisis, it does make some significant contributions to the appropriate distribution of health resources.[12]

The Downside

All social and economic programs have potential pitfalls which must be guarded against. CON is no exception. Under CON there are potential bureaucratic delays in needed programs. The CON process involves review of proposals by professional staff, affected parties, committees, Health Services Council, and the Director of Health. This takes time, often substantial time. CON also has the potential of stifling innovations. There is always the risk that CON will respond too conservatively to new ideas. In addition, CON has the potential of over-politicizing health issues. If CON degenerates into power politics rather than focusing on the merits of proposals, then the process loses its reason for being. Further, there is the potential that well-established providers could use the CON process to block the entrance of legitimate competitors into the market and maintain the "status quo." CON was intended to promote the public interest, not to protect the provider industry. Also, CON has the potential of serving as a prop for an outdated health-care financing system. To the extent that CON protects traditional reimbursement mechanisms against the winds of progressive change, it becomes excessively conservative. Finally, CON has the potential of protecting inefficient, outdated, and weak providers. To the degree that this happens, CON serves as a roadblock to the natural evolution of the health-care industry.

In short, CON is not without risks. CON embodies the potential for counterproductive impacts. These dangers must be constantly recognized and consciously avoided.

Innovations

There is no reason why CON cannot change as better ways are identified to conduct the process. In fact, a significant number of constructive changes have been made in the Rhode Island CON program in recent years.

In 1984, as a result of the work of the Special Legislative Commission to Study Health Care Capital Expenditures — the Carcieri Commission, a "CONCAP" was added to the CON process by the General Assembly.[13] CONCAP is a limit on hospital interest and depreciation expenses that can be approved in the CON process. For the first time, CON hospital capital expense reviews are conducted within the context of an overall budgetary constraint. Now, both community need and affordability must be addressed.

In 1985, three important legislative changes were made in the CON process. CON was removed as a precondition to the establishment of new HMOs in the State. This change was designed to facilitate the development of HMOs in Rhode Island consistent with two State Health Plans.[14,15] A "Request for Proposal" (RFP) feature was added to the CON process. This provision adds a proactive component to a process which has been criticized for being solely reactive. Now, the Director of Health can stimulate the development of competing CON proposals to address a clearly identified or potential need. In fact, in recent years the Director of Health has issued CON RFPs for the following services: 1) Magnetic Resonance Imaging (MRI), 2) home health care and rehabilitation care. A "pro-innovative" criterion was also added to the CON process. This criterion permits the approval of innovative, cost-effective proposals, even if the absolute quantitative community need has been met. This "pro-innovative" criterion should help to avoid some of the potentially stifling effects of the CON program.

In 1986, state legislation raised the CON review thresholds over a three-year period to the federal standards ($600,000 for capital, $400,000 for equipment and $250,000 for new services). This is another change that was endorsed by the Special Legislative Commission to Study Health Care Capital Expenditures — the Carcieri Commission.[16] Higher thresholds will help to keep CON focused on those proposals which will have

the biggest financial impact on the health care system.

Thus, there is ample demonstration that CON is not cast in concrete. Constructive changes have been made to the CON process in the past, and additional salutary changes can and should be made to the CON process in the future.

Potential Modifications

At the present time, there are a number of potential modifications to the CON program which are being given serious consideration. First, CON should cover specified advanced medical technology services regardless of their costs (eg, DSA, cardiac catheterization, MRI). The development of advanced medical technology deserves careful public study and review. The number and locations of advanced medical technology sites will have a critical impact on the quality, cost and accessibility of medical care in Rhode Island.

Second, nonclinical programs should perhaps be exempted from the CON process. When CON began in 1968 there was no prospective hospital reimbursement program (MAXICAP) to limit total community hospital expenditures in Rhode Island; and, there was no Diagnostic Related Groups (DRG) system of hospital reimbursement for Medicare. Further, at that time, there were no HMOs and there were no managed access programs. Today, it is not necessary for CON to carry the sole burden of cost control. If nonclinical proposals such as parking lots, boilers, and telephones were removed from the program, CON would be much less burdensome. With nonclinical programs removed, CON could truly concentrate on the major clinical proposals of our time.

Third, a fast-track system should be established within CON to expedite the review of routine proposals such as the many nursing-home bed reclassifications. The ability to fast-track noncontroversial proposals would make the CON process less frustrating and less arduous for all involved. These first three ideas were discussed during the 1987 session of the Rhode Island General Assembly.

There are two additional CON possibilities which should receive careful exploration. Perhaps nonhospital proposals should be included in the CONCAP annual limit on interest and depreciation expenses so that alternative service-delivery tradeoffs could be considered explicitly and all major health-facility capital developments would be subjected to a common budgetary constraint. Possibly the CONCAP should also be set for a three-or-five year period of time, rather than for one year at a time. This change would reflect the lumpy nature of health facility capital expenditures over time; and it could help to strengthen institutional long-range planning.

In any event, we should continue to evaluate critically the CON process and make sensible modifications during the years ahead.

Concluding Perspectives

This is the most volatile health-system environment that we have ever seen. Change in the health system today is very rapid and somewhat unpredictable. Therefore, this would be exactly the wrong time to abandon CON. CON is a powerful health-system management tool. This is certainly no time to be throwing such tools away.

At this point, we still need CON to aid us in health-care cost control and quality assurance. Health service inflation is now increasing at the rate of 7.7 per cent per year. This is almost six times greater than the current general inflation rate of approximately 1.3 per cent![17] Analysis indicates that in inflation adjusted dollars health-care spending has actually been accelerating since 1980![18]

Some people believe that the growing market penetration of HMOs will ultimately eliminate the need for CON since HMOs have a built-in incentive to conserve on expensive health care. This is a possibility. However, with only about 15 per cent of the population currently enrolled in HMOs, it is much too premature to be talking about the obsolescence of CON. The states which have discarded CON in recent months and years have experienced frightening expansions of hospital and nursing home beds (eg, Utah, Arizona, Indiana).[19-21]

No one is particularly enamored by regulation. It is not a terribly uplifting experience. Nevertheless, regulatory programs are a critical component of the system of checks and balances in our free enterprise system.

References

[1] Joseph A. Chazan, "Certificate of Need: A Concept Whose Time Has Passed, The Competition of the Marketplace Should be Allowed to Function without Governmental Interference," Rhode Island Medical Journal. 69:273-275, 1986.

[2] Rhode Island Department of Health, Health Planning and Resources Development, Technical Report No. I6, The 1967 Brosco Commission, May 1979.

[3] Ibid. p. 48.

[4] Ibid. p. 49.

[5] Intergovernmental Health Policy Project, The George Washington University, State Health Notes "CON Changes Taper Off." 67:1, 1986.
[6] ALPHA Center, ALPHA CENTERPIECE, "Deregulation is Growing Trend for State CON Programs," February 1986, pp. 2 and 3.
[7] U.S. Department of Health and Human Services, Public Health Service, National Center for Health Statistics, Health United States 1985, DHHS Pub. No. (PHS) 86-1232, Hyattsville, Maryland (December 1986), p. 116.
[8] Gerald Riley and James Lubitz, "Outcomes of Surgery Among the Medicare Aged: Surgical Volume and Mortality," Health Care Financing Review. 8:23-34, 1986.
[9] Ann Barry Flood, W. Richard Scott and Wayne Ewy, "Does Practice Make Perfect? Part I: The Relation Between Hospital Volume and Outcomes for Selected Diagnostic Categories, and Part II: The Relation Between Volume and Outcomes and Other Hospital Characteristics," Medical Care 22:98-125, 1984.
[10] Joyce V. Kelly and Fred J. Hellinger, "Physician and Hospital Factors Associated with Mortality of Surgical Patients," Medical Care. 24:785-800, 1986.
[11] U.S. Department of Health and Human Services, Public Health Service, National Center for Health Services Research and Health Care Technology Assessment, Competition Among Hospitals: Market Structure and Its Relation to Utilization, Costs and Financial Position, Hospital Studies Program, Hospital Cost and Utilization Project, Research Note 7, August 1986.
[12] John T. Tierney, William J. Waters and William Rosenberg, "Certificate-of-Need-No Panacea but Not Without Merit," Journal of Public Health Policy. 3:178-181, 1982.
[13] Special Legislative Commission to Study Health Care Capital Expenditures, Representative Anthony J. Carcieri, Chairman, Final Report, January 1983.
[14] Rhode Island Statewide Health Coordinating Council, Rhode Island Health Plan Part I and Part II, May 1980.
[15] Rhode Island Statewide Health Coordinating Council, Rhode Island Health Plan 1983-1987, January 1983.
[16] Special Legislative Commission to Study Health Care Capital Expenditures, Representative Anthony J. Carcieri, Chairman, Report to the General Assembly, May 1986.
[17] Warren Brookes, "The big health-care cut," The Providence Journal Bulletin, January 18, 1987.
[18] Uwe E. Reinhardt, "There's Still no Cure for Exploding Health Care Costs," Business Week, September 22, 1986 reported in MEDICAL BENEFITS, October 15, 1986.
[19] American Medical News, "Arizona Deregulation Spurs Growth in Medical Facilities," September 19, 1986.
[20] Long Term Care Management 15, "Repeal of CON Laws Brings Fears of Lower Occupancy Rates." 22:7, 1986.
[21] Long Term Care Management 15, "Arizona Nursing Home Construction 'Phenomenal' Since Deregulation." 19:3, 1986.

75 Davis Street
Providence, RI 02908

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

PRIME COMMERCIAL BUILDING

★★★★★★★★★★

IDEAL FOR
—PRIVATE EMERGENCY ROOM—
—MEDICAL LABORATORY—
—DOCTORS OFFICES—
—INVESTMENT—

★★★★★★★★★★

6,000 SQUARE FEET PLUS RENTAL INCOME

★★★★★★★★★★

DOWNTOWN WEST WARWICK

$295,000

CALL THE OWNER AT 461-1500

AIM HIGH

A PRESCRIPTION FOR PHYSICIANS

BOTHERED BY:

★ Too much paperwork?
★ The burden of office overhead?
★ Malpractice insurance costs?
★ Not enough time for the family?
★ No time to keep current with technology and new methods?
★ No time or money for professional development?

JOIN THE AIR FORCE MEDICAL TEAM; WE'LL PROVIDE THE FOLLOWING:

★ Competent and dedicated professional staff.
★ Time for patients and for keeping professionally current.
★ Financial security, a generous retirement for those who qualify.
★ If qualified, unlimited professional development.
★ Medical facilities all around the world.
★ 30 days of vacation with pay each year.
★ Complete medical and dental care.
★ Low cost life insurance.

Want to find out more? Contact your nearest Air Force recruiter for information at no obligation. Call

Ssgt A. J. Avila
401-528-4044 collect

AIR FORCE

Diagnosis, Significance, and Treatment of Neonatal Seizures

Recommendations Are Made For An Approach To Suspected Seizures Based On Updated Information

Edwin L. Zalneraitis, MD

Seizures are thought to be the most common manifestation of neurologic disease in the newborn. Appropriately, these phenomena have been and continue to be studied by many researchers. The resultant body of knowledge has recently been the topic of several general reviews that can be recommended to the reader.[1-3] This review recapitulates and updates the status of selected issues of particular relevance in the practical care of newborn infants.

The initial discussion addresses the problem of identification of seizures in the face of immaturity. Recognizing persistent uncertainty in diagnosis, consideration will then be given to the possible importance of suspected neonatal seizure. Finally, based on the potential consequences of the seizures, a discussion of the nature and duration of intervention will be presented.

Diagnosis:

The reported occurrence rates of neonatal seizures vary widely from 0.15 per cent in a general population[4] to 20 per cent of a high-risk premature population prior to 1975.[5] In the National Collaborative Perinatal Project, one in every 200 infants was diagnosed as having had a seizure in the first 28 days of life.[6] For 1985-86, in our neonatal intensive care unit (NICU), 6.3 per cent of all infants were reported to have had seizures. There are many possible reasons for the wide variability in the reported frequency of seizures in newborn infants. There are, for example, notable differences in risk factors and management for the populations studied; but there are also differences in and difficulties with the ways in which the diagnosis of neonatal seizure was established. Although difficulty in recognition of seizures is not unique to the newborn, the incomplete development of the nervous system in both premature and term infants makes the task considerably more difficult. The details of this immaturity are beyond the scope of this review, but the result is a much different range of behaviors than is seen in more mature individuals. These activities may be partial and paroxysmal in nature, even when they are not thought to result from seizures. Therefore, it is often difficult to distinguish them from the suspected seizures. Moreover, the ictal manifestations seem to be unique as well. As a result, Volpe[7] has proposed a separate classification for neonatal seizure, seen modified in Table 1.

Subtle seizures are thought to be the most common type of neonatal seizures. Estimates of frequency are not offered, but they are thought to occur in most neonates having seizures even if other seizure types are present.[7] The movements may include paroxysmal nystagmus, blinking, pedaling, swimming, rowing, bicycling, or buccal-lingual movements. Other spells may include downward eye jerking, hyperpnea, vasomotor changes, or single limb posturing. These have

Edwin L. Zalneraitis, MD, is Assistant Professor of Pediatrics and Neurology at University of Connecticut Medical School and Attending Pediataric Neurologist at John Dempsey Hospital, University of Connecticut Health Center.

Table 1. Classification of Neonatal Seizures

1. **Subtle** — isolated, intrusive automatisms such as abnormal eye movements, sucking, pedaling, rowing or swimming movements
2. **Generalized Tonic** — extremity extension resembling decerebrate posturing
3. **Multifocal Clonic** — clonic jerking migrating from extremity to extremity
4. **Focal Clonic** — clonic jerking that is repetitive and localized
5. **Myoclonic Seizures** — single or multiple, concerted, flexion jerks of the extremities

been linked to seizure by the clinical setting in which they occur, the observed interruption of other neonatal activity, electroencephalographic (EEG) studies, and response to anticonvulsant medication.[3] However, these associations were not consistently demonstrated in the studies reviewed.[8-10] On the contrary, time-synchronized video-EEG (TSVE) monitoring revealed a very limited association between electrographic discharge and subtle seizure manifestations.[11, 12] It appears that at least some of the abnormal activity may not be seizure activity, but rather a decreased regulation of the brain stem. Concurrent electrical suppression seen on the EEG is cited as evidence of this.[11, 12] Pending further studies, the diagnosis of subtle seizure remains uncertain, and its significance and management must be considered in light of this.

Infants suspected of having convulsive apnea may be considered to have a variation of subtle seizure. Apnea is particularly common in newborn, especially premature infants. Conversely, seizures often disturb respiration. Therefore, the question of convulsive apnea is more frequently an issue than a reality. Electrographic monitoring studies instruct us that most infants with convulsive apnea have other recognized seizure-like activity.[8, 10, 12] However, apnea can present as the sole or first manifestation of suspected seizure activity in the newborn.[8] These seizures may be distinguished by the fact that they invariably occur during Rapid Eye Movement (REM) sleep, and are highly associated with focal, monorhythmic (usually alpha frequency) discharges that are temporal rather central in location. A variety of other electrical paroxysms have been described, but they are not specific for this seizure type. The clinical presentation of the apnea seems to be non-specific as well, though Fenichel et al reported that early bradycardia was much more likely in non-convulsive than in convulsive apnea.[13] Wantanabe et al failed to confirm this finding.[8]

Generalized tonic seizures are reported to be the second most common seizure type in newborns.[3] They consist of paroxysmal extensor and less commonly flexor posturing of the extremities that resembles decerebrate and decorticate posturing. The diagnostic dilemma is that, with the expected absence of significant cortical contribution in this age group, the postures seen may be normal responses to environmental stimulation. TSVE studies also failed in this situation to confirm a substantial association of electrographic discharge and tonic posturing.[11, 12] As with the subtle seizures, EEG suppression is better correlated with such events, and they may be viewed as a brainstem release phenomenon as well. These paroxysms also require further investigation before conclusions can be drawn.

Clonic seizures are reportedly more common in more mature neonates.[3] Multifocal clonic seizures are described as migrating clonic jerks that occur in a non-Jacksonian pattern. These often correlate with irregular multifocal changes on the EEG. Focal clonic seizures are less common and occur in the setting of correlative, focal EEG, radiologic, and pathologic changes. The lesions are typically cerebral infarctions, and both ultrasound and computerized tomography may be needed to properly investigate the focus.[14-18] It is important to evaluate for other focal treatable diseases such as subdural hematoma or empyema. Such lesions are not common, but their expected location near the surface of the brain often mandates diagnosis by computerized tomography due to current limitations in ultrasound technology. Clonic phenomena closely correlate with electrographic discharge on TSVE, and appear to be a genuine manifestation of seizure activity in neonates.[11, 12] Here, the major issue in diagnosis usually is to distinguish clonic seizures from jitteriness. Table 2 summarizes a typical scheme to aid in this differentiation. The

Table 2. Distinguishing Neonatal Seizure from Jitteriness

Clinic Manifestation	Jitteriness	Seizures
Stimulus sensitive	Yes	rarely
Velocity of movement	rapid	slow
Four extremity involvement	often	rare
Flexion — extension	equal	fast and slow
Cease with passive flexion	always	rarely
Gaze abnormality	inconsistent	more consistent
AED response	less likely	more likely

jittery baby typically has a rapid stimulus-sensitive tremor of all four extremities. This activity is often eliminated by gentle passive flexion; and it is not typically associated with gaze abnormality or response to antiepileptic drugs (AED). It should be cautioned that the potential etiologies for jitteriness and seizure are similar, and the main purpose of distinguishing them is to discern the need for AED, not to diminish concern for causative processes.

Myoclonic seizure, the final seizure type in the proposed classification, may be particularly troublesome from a diagnostic point of view. Myoclonus has been reported to be the least common manifestation of seizure activity in neonates, but it has often been associated with severe encephalopathy.[3] Accordingly, earlier studies reported severe EEG disturbances in extremely ill newborn infants with myoclonus.[19,20] However, TSVE[11,13] and detailed study of a standard EEG in newborns with myoclonus[21] have failed to correlate the myoclonus with EEG seizure discharge. Moreover, myoclonus frequently occurs in neonates, especially prematures, free from any apparent neurologic disturbance or EEG alteration. This has been recognized as benign myoclonus of the newborn, and caution is advised to avoid unnecessary testing and therapy in such infants.[22] When pathologic myoclonus does occur, the EEG-myoclonus correlations seen are similar to those noted in adults (cortical, reticular, and segmental). Such pathologic myoclonus seems to reflect neurologic dysfunction at various levels of the neuraxis, but it has not been recognized as seizure.[21] For now, myoclonus should be considered most often a non-convulsive event, and the decision to pursue this activity diagnostically or therapeutically rests upon the recognition of its association with probable neurologic insults. This, then, is another problem in need of future study.

It is evident that the discussion of the proposed classification of neonatal seizures has focused on the limitation of direct observation and routine EEG as revealed by continuous monitoring techniques such as TSVE. However, it should also be recognized that continuous EEG monitoring is a time-consuming, expensive, and unstandardized technique; and efforts have been made to simplify and refine such monitoring. An example of this is the use of cassette monitoring of EEG for newborns with suspected seizure activity, but no electrographic correlate on routine EEG. Twenty-four hour, three-channel, tape cassette recordings on such infants have been shown to be helpful in detecting EEG seizures, particularly if a suspicious spell has occurred within 24 hours of the recording.[23] Development of more practical diagnostic monitoring techniques such as this one will facilitate improved understanding of neonatal seizures. Other important uses for such technology include evaluation of newborn infants with apnea and neonates subjected to pharmacologic neuromuscular blockade. In the latter situation, continuous EEG monitoring demonstrates that most, though not all, infants having seizures while paralyzed will have periodic, otherwise unexplained fluctuations in vital signs or oxygenation.[24,25] If practical electrophysiologic monitoring is not available, seizure evaluation or therapy may be used just for infants of this type to avoid administering prophylactic AED where not necessary. Not only does this create a dilemma for practical-care situations, but under these circumstances the importance of these events and the efficacy of therapy remain obscure.

Finally, with regard to recognition of neonatal seizure, it is implied by the foregoing discussion that the establishment of this diagnosis is confounded by the lack of a consensus as to what constitutes a neonatal seizure. Seizures in general, including neonatal seizures, have been defined primarily by observed clinical manifestations. The classification reviewed here is the most widely accepted, is based on observed manifestations, and makes the important assumption of the uniqueness of seizure events in the neonate. However, its validity has never been established, and more recent studies indicate that it may be insufficient for this age group. This is the focus of the recent letters of Mizrahi and Abroms,[26] and it is particularly apparent from their comments that the most accurate method of diagnosing and classifying neonatal seizure must be determined as a prerequisite to further understanding of these events. Observed manifestations may have to be augmented by information gained through EEG techniques which have been reviewed in detail by Holmes.[1]

Significance

The important reasons for recognizing seizure-like activity in neonates may be divided into three categories. First, these events often occur with significant illnesses, particularly neurologic diseases. The associated disorders sometimes indicate a need for specific therapy, often on an urgent basis. Second, the presence of seizures and associated processes appear to provide prog-

nostic information. Third, suspected neonatal seizures may be harmful to the newborn directly from deleterious effects of the seizures themselves.

Considering *diagnostic* importance, Table 3 shows the primary diagnoses for the 47 infants in our NICU in 1985-86 who were thought to have seizures. The group with presumed asphyxia is further delineated in Table 4. This information is similar to that found by others,[3, 6, 19, 27, 28] but with the conspicuous absence of several categories (discussed below). The data illustrates the point that, though the differential diagnosis for neonatal seizure is large, the vast majority of cases occur in a relatively small number of settings. In addition, it is also uncommon now to fail to recognize a cause for neonatal seizures.[1-3]

As shown in Table 3, asphyxia has been designated as the most common cause of seizures occurring as part of an hypoxic-ischemic encephalopathy.[3, 27-30] This diagnosis, however, is generally inferred from investigations suggesting ischemic compromise and encephalopathy in the infant. Direct measurement of cerebral ischemia has not been obtained, and there is nothing specific about the manifestations of the encephalopathy. It is important, therefore, to consider other processes presenting with seizures and acute encephalopathy in this age group. These include central nervous system infection, trauma, intracranial hemorrhage, metabolic derangements and rarely the neurocutaneous diseases incontinentia pigmenti and tuberous sclerosis. An important, though rare, cause of early encephalopathy with seizures is the inadvertent injection of local anesthetic into the infant's scalp while attempting local anesthesia for episiotomy.[31, 32] This condition should be considered in the setting of early loss of pupillary reaction to light and loss of extraocular movements. The clinician should check the infant carefully for needle marks, and prompt treatment should include diuresis with urine acidification.[32] Another

Table 3. Associated Diagnoses with Seizure. N = 47 (1985-86)

Diagnosis	Number	Percent
Asphyxia	35	74
CNS infection	6	13
CNS malformation	4	9
CNS trauma	1	2
Primary ICH*	1	2

* ICH = intracranial hemorrhage

Table 4. Asphyxia and Seizure. N = 35 (1985-86)

Maturity	Type of Insult	Number	Percent
Term	acute	19	55
	chronic	0	0
Premature	acute	5	14
	chronic	11	31

condition that may be neglected in this setting is hypertension, particularly in view of the common focus on shock and ischemia. The importance of recognition of hypertension and appropriate therapy is emphasized.[33]

Although metabolic derangements as a cause for suspected seizures are absent in our recent series, this does not diminish the importance of considering these disorders. Their recognition commonly leads to significant therapeutic, prognostic, or genetic considerations. For example, in the setting of presumed asphyxic encephalopathy, 15 per cent of our infants developed hypoglycemia, while 21 per cent had hypocalcemia. It should be noted, however, that as opposed to observations in earlier studies,[19, 34] it is uncommon at present to have seizures diagnosed as secondary to isolated glucose, calcium, or electrolyte abnormalities. Likewise, nutritional deficiencies, such as late pyridoxine depletion, have been virtually eliminated, while much rarer conditions such as pyridoxine dependency have been recognized. This disorder is typically diagnosed by a trial of 50 to 100 mg of pyridoxine inducing a dramatic halt to refractory seizures. More recently it has been recognized that more than 100 mg may be required, while no toxicity of higher doses has been discerned.[35] Although our recent series did not contain any patients with inborn errors of metabolism, these rare but important conditions can be causes for seizures in newborn infants. Aminoacidopathies, organic acidemias, peroxisomal disease, and mitochondrial disorders should be considered as possible causes, while lysosomal disease is unlikely. Finally, drug withdrawal, though frequently associated with neurologic signs such as jitteriness, should be viewed as a rare metabolic cause of seizure.[36]

Finally, in this consideration of the diagnostic significance of neonatal seizures, seizure syndromes are recognized in apparently well newborns. A syndrome of dominantly inherited benign neonatal seizures has been identified. Frequent seizures, as many as 10 to 20 per day, are noted beginning on the second or third day

of life (hence the appellation "third day fits"). They last one to six months, and the outcome is benign except for increased risk of seizures (11 per cent) later in life.[37,38] A syndrome of nonfamilial seizures beginning late in the first week of life has also been described in otherwise healthy infants. These have been called fifth day fits after the peak time of their recognition. They are typically multifocal clonic seizures lasting less than 24 hours, with a maximum of 15 days duration.[39] A relationship between these spells and low cerebrospinal fluid zinc levels has been reported,[40] but the outcome has been uniformly benign. Caution is urged in diagnosing seizures in healthy infants, and study for additional syndromes of neonatal seizures is encouraged.

Knowledge of the *prognosis* for infants thought to have neonatal seizures has been valuable in formulating therapeutic decisions, and in assessing the possible impact of these events and their associated disorders. Despite the fact that fewer seizures are related to primary metabolic imbalance and more to direct neurologic insult, the prognosis for these infants appears to be either unchanged[28] or improving[3] with improved neonatal care. Prior to the onset of neonatal intensive care, the National Collaborative Perinatal Project recorded a mortality of 33 per cent and significant morbidity of 30 per cent in survivors,[6] while Rose and Lombroso reported 30 per cent morbidity and 20 per cent mortality[19] for infants thought to have seizures. With intensive care, Bergman et al detected a similar, approximately 50 per cent combined mortality and morbidity.[28] In our nursery, an earlier report of 74 infants with a diagnosis of seizure had a mortality of only 8 per cent, but a morbidity of 46 per cent.[41] Our recent series of patients from 1985-86 had a mortality of 38 per cent but a morbidity of only 15 per cent.

Outcome for infants with seizures has been linked specifically to etiology, EEG, and seizure type. As anticipated, prognosis is most closely related to the cause of the seizures. Brain malformations have been uniformly associated with adverse outcome, while asphyxia, intraventricular hemorrhage, and central nervous system infection all have had greater than 50 per cent morbidity.[3] In contrast, primary metabolic imbalance and subarachnoid hemorrhage, as well as the seizure syndromes in healthy neonates, have a favorable prognosis. After etiology, EEG is recognized as the next best indicator of outcome. Ictal discharge, but more importantly background activity during the acute neonatal illness, provide the basis for these judgements.[8,10,19,20,41,42] However, caution is required in interpreting periodic EEG background in premature infants where this can be found in normal infants.[3] Lastly, the controversial seizure types — subtle, tonic, and myoclonic — have been most closely linked to adverse outcome.[6,8,9,43] This is not unexpected, since these behaviors are seen in infants with greater immaturity, severity of illness, and incidence of identified neurologic insult. The direct role of these phenomena in establishing prognosis is unclear and the available data are also unreliable due to the diagnostic dilemmas previously discussed.

Finally, these seizures may be important due to *direct injury* related to their occurrence. This is suggested by studies indicating increased risk of an unfavorable outcome with more prolonged, persistent, and frequent seizures.[28,44] However, more severe neurologic insults are also related to the difficulty in seizure control. There are no prospective controlled studies to refute contentions that the outcome may be due solely to primary neurologic disease without additional direct harm from the seizures. Though such controlled studies are clearly needed, other evidence does exist to suggest that seizures may cause direct harm to newborns. As already discussed, seizures in infants can interfere with ventilation. This is an established treatable source of potential harm from seizures that fortunately is rare. Likewise, very frequent or prolonged seizures can interfere with nutritional progress. Physiologically, alterations in blood pressure, cerebral blood flow, and intracranial pressure have been shown to occur in newborns with seizures, even when pharmacologically paralyzed or with subtle seizures.[45-47] Biochemically, infants have been shown by nuclear magnetic spectroscopy to have reduced cerebral high-energy phosphate compounds during subtle seizures.[48] This has also been demonstrated in paralyzed experimental animals. Other experimental models have shown depletion of brain glucose and impairment of brain protein, DNA, RNA, and cholesterol synthesis.[1-3] Though not definitive, the evidence is compelling enough to suggest that prompt therapeutic efforts should be instituted when seizures are diagnosed in neonates. However, this assessment does not obviate the need for appropriately controlled studies, particularly in the face of some experimental evidence that anti-epileptic drugs (AED) may be harmful to the developing nervous system.[49,50]

Treatment

Though there may be debate about the urgency and need to treat neonatal seizures,[51] there is no doubt that therapy always begins with supportive care that attends to the infant's vital functions. This should be followed by prompt diagnosis and treatment of causative processes if possible. Finally, AED administration to prevent further seizures is suggested. Table 5 depicts one possible approach to therapy. It should be noted that administration of glucose, calcium, magnesium, and pyridoxine are no longer performed as routine "diagnostic trials" in most centers. With the rapid availability of bedside and laboratory methods to monitor these constituents, therapy is reserved for recognized abnormalities or for cases of refractory seizures.

Table 5. Treatment of Neonatal Seizures

1. Supportive care: maintenance of vital function
2. Treatment of diagnosed cause as possible
   a. neurologic insults: infection, trauma, toxic injection, etc.
   b. metabolic imbalance (recognized or for refractory seizure)
      1. dextrose, 10% solution: 2 ml/kg, IV
      2. calcium gluconate, 5% solution 4 ml/kg, IV
      3. magnesium sulfate, 50% solution: 0.2 ml/kg, IM
      4. pyridoxine: 100-200 mg, IV
      5. maintenance of above
3. Anti-epileptic drugs
   a. phenobarbital 20-30 mg/kg load; 3-5 mg/kg/24 hrs, IV, IM, PO
   b. phenytoin 20 mg/kg load; 4-6 mg/kg/24 hrs, IV only
   c. other AED — lorazepam, primidone, paraldehyde, diazepam

There is no evidence that any one AED is superior in controlling neonatal seizures. Phenobarbital is usually the drug of choice. There is a high predictability of therapeutic success, and little apparent adverse consequence when given properly. Although 20 mg/kg has been suggested as an intravenous (IV) loading dose,[52] it has been shown that 30 mg/kg more reliably establishes desired therapeutic drug levels without apparent adverse effect in term neonates.[53] This medication has a serum half-life of greater than 100 hours,[52, 53] and needs only to be given once daily. It can be also absorbed well either intramuscularly or orally. Initially, a maintenance dose of 3 mg/kg/day is usually satisfactory. After two weeks, an increase to 4-5 mg/kg/day may be required. Serum drug levels should be monitored early in the course.

Phenytoin is typically the second medication used. It is effective, but IV administration is required due to poor oral absorption of the drug by the newborn.[52] If used orally, the dose required increases from 4-6 mg/kg/day IV to a forbidding dose of 15-20 mg/kg/day.[54] The intravenous preparation is very alkaline and can make intravenous access difficult to maintain. This, combined with possible deleterious effect on the developing nervous system,[50] should lead to caution in its use.

The use of additional medications becomes increasingly problematic due to increased potential toxicity and questionable benefit. However, there are studies to suggest the efficacy of other AED for refractory neonatal seizures. Primidone has been reported to be useful for such seizures.[55] The drug is given as a 15-25 mg/kg load, followed by 12-20 mg/kg/day. It must be given orally, and, though it does not convert to phenobarbital in newborns, it does interfere with barbiturate metabolism. Concomitant phenobarbital therapy should be monitored carefully, and the dose reduced accordingly. Paraldehyde, given as a bolus of 200 mg/kg IV and maintained at 16 mg/kg/hour, has been effective at serum levels greater than 10 mg/dl. An additional 200 mg bolus can be given safely to newborns over one hour old.[57] Rectal paraldehyde has not been studied in this age group, and should be used with care to avoid rectal and perianal complications. The rectal dose, 0.3 ml/kg in an equal volume of oil, can be given when IV administration is not practical. Also, it is important to remember the significant pulmonary elimination of this drug. Control has been reported using lorazepam for 7 neonates with refractory seizures.[56] An IV dose of 0.05 mg/kg was given without observable adverse effect. In contrast, Volpe has described the potential drawbacks of neonatal diazepam use.[3] Uniform efficacy of this AED has been reported when delivered in a dilute saline solution, but significant somnolence was noted in all infants.[58] Lorazepam appears to be preferable if a benzodiazepine drug is contemplated, and diazepam should be used cautiously in jaundiced neonates when delivered in its benzoate form. This vehicle has been shown to dissociate bilirubin from albumin, raising the risk of kernicterus.

Finally, with regard to treatment, the duration of therapy is a matter of increasing controversy. Shorter duration of therapy has been recommended based on the low risk of late recurrence.[28, 59] The neurologic examination, cause of the seizure, and EEG have all been found helpful in recognizing the risk of recurrence.[8, 28, 59] Infants with a normal neurological examination and

normal or mildly abnormal EEG have been removed from AED therapy with less than a 10 per cent risk of late recurrence. Our experience corroborates this, and there is no established rate of risk of late recurrence. It is recommended that in stable infants with normal examinations and non-epileptiform EEG showing good background activity, AED therapy be discontinued when they are seizure free for two weeks. Gal et al[59] feel that this time can be shortened to three to five days if the infants are stable and the cause of the seizure is corrected. Therapy for infants with unfavorable diagnoses such as brain malformation is continued.

Conclusions

The diagnosis of neonatal seizure must be made carefully, and even then the validity of the diagnosis remains in doubt. When neonatal seizures are suspected, neurologic processes should be identified and treated whenever possible. Supportive therapy and frequently short-term AED therapy are also indicated. Well-defined controlled prospective clinical studies to allow for better identification, prognostication, and rational therapy for neonates with seizures should be undertaken.

Acknowledgments

I wish to thank Dr Gregory Holmes for his advice and criticism. I am also grateful to Mrs. Susan DiCorpo for her invaluable assistance in preparing this manuscript.

References

[1] Holmes GL. Neonatal Seizures. In Holmes GL. The Diagnosis and Management of Seizures in Childhood. Philadelphia, W.B. Saunders, 237-61, 1987.

[2] Painter MJ, Bergman I, Crumrine P. Neonatal seizures. Pediatr Clin North Am 33:91-109, 1986.

[3] Volpe JJ. Neonatal Seizures. In Volpe JJ. Neurology of the Newborn. 2nd ed. Philadelphia, W.B. Saunders, 129-57, 1986.

[4] Eriksson M, Zetterstrom R. Neonatal convulsions. Acta Pediatr Scand 68:807-11, 1979.

[5] Seay AR, Bray PF. Significance of seizures in infants weighing less than 2500 grams. Arch Neurol 34:381-82, 1977.

[6] Holden KR, Mellitis ED, Freeman JM. Neonatal Seizures: 1. correlation of prenatal and perinatal events with outcomes. Pediatarics 70:165-76, 1982.

[7] Volpe JJ. Management of neonatal seizures. Crit Care Med 5:43-49, 1977.

[8] Wantanabe K, Hara K, Miyazaki S, et al. Apneic seizures in the newborn. Am J Dis Child 136:980-84, 1982.

[9] Knauss TA, Carlson CB. Neonatal paroxysmal monorhythmic alpha activity. Arch Neurol 35:104-07, 1978.

[10] Willis J, Gould JB. Periodic alpha seizures with apnea in a newborn. Dev Med Child Neurol 22:214-22, 1980.

[11] Mizrahi EM, Kellaway P. Characteristics of seizures in neonates and young infants by time-synchronized EEG/polygraphic/video monitoring. Ann Neurol 16:383, 1984.

[12] Shewmon DA. Dissociation between cortical discharges and ictal movements in neonatal seizures, Ann Neurol 14:368, 1983.

[13] Fenichel GM, Olson BJ, Fitzpatrick JE. Heart rate changes in convulsive and nonconvulsive neonatal apnea. Ann Neurol 7:577-82, 1980.

[14] Barmada MA, Moossy J, Shuman RM. Cerebral infarcts with arterial occlusion in neonates. Ann Neurol 6:495-502, 1979.

[15] Mannino FL, Trauner DA. Stroke in neonates. J Pediatr 102:605-09, 1983.

[16] Hill A, Martin DJ, Daneman A et al. Focal ischemic cerebral injury in the newborn: diagnosis by ultrasound and correlation with computed tomographic scan. Pediatrics 71:790-93, 1983.

[17] Clancy R, Malin S, Laraque D. Focal motor seizures heralding stroke in full-term neonates. Am J Dis Child 139:601-06, 1985.

[18] Levy SR, Abroms IF, Marshall PC et al. Seizures and cerebral infarction in the full-term newborn. Ann Neurol 17:366-70, 1985.

[19] Rose AL, Lombroso CT. Neonatal seizure states: a study of clinical, pathological, and electroencephalographic features in 137 full-term newborn babies with a long-term follow-up. Pediatrics 45:404-25, 1970.

[20] Harris R, Tizzara JPM. The electroencephalogram in neonatal convulsions. J Pediatr 57:501-20, 1960.

[21] Scher MS. Pathologic myoclonus of the newborn: electrographic and clinical correlations. Pediatr Neurol 1:342-48, 1985.

[22] Coulter DL, Allen RJ. Benign neonatal sleep myoclonus. Arch Neurol 39:191-92, 1982.

[23] Bridgers SL, Ebersole JS, Ment LR et al. Cassette Electroencephalography in the evaluation of neonatal seizures. Arch Neurol 43:49-51, 1986.

[24] Goldberg RN, Goldman SL, Ramsay ER et al. Detection of seizure activity in the paralyzed neonate using continuous monitoring. Pediatrics 69:583-86, 1982.

[25] Eyre JA, Oozeer RC, Wilkinson AR. Continuous electroencephalographic recording to detect seizures in paralyzed newborn babies. Br Med J 286:1017-18, 1983.

[26] Mizrahi EM, Abroms IF. Neonatal seizures: the need for precise clinical characterization. Ann Neurol 21:312-13, 1987.

[27] Goldbert HJ. Neonatal convulsions — a 10 year experience. Arch Dis Child 58:976-78, 1983.

[28] Bergman I, Painter MJ, Hirsch RP et al. Outcome in neonates with convulsions treated in an intensive care unit. Ann Neurol 14:642-47, 1983.

[29] Hopkin IJ. Seizures in the first week of life: a study of aetiological factors. Med J Australia 2:647-51, 1972.

[30] Fenichel GM. Hypoxic-ischemic encephalopathy in the newborn. Arch Neurol 40:261-66. 1983.

[31] Kim WY, Pomerance JJ, Miller AA. Lidocaine intoxication in the newborn following local anesthesia for epesiotomy. Pediatrics 64:643-45, 1979.

[32] Hillman L, Hillman R, Dodson WE. Diagnosis, treatment and follow-up of neonatal mepivicaine intoxication secondary to paracervical and pudendal blocks during labor. J Pediatr 95:472-77, 1979.

[33] Mare S. Hypertensive encephalopathy: A cause of neonatal seizures. Am J Dis Child 137:32-33, 1983.

[34] Brown JK, Cockburn F, Forfar JJO. Clinical and chemical correlates in convulsions of the newborn. Lancet 1:135-39, 1972.

[35] Bankier A, Turner M, Hopkins IJ. Pyridoxine dependent seizures — a wider clinical spectrum. Arch Dis Child 58:415-18, 1983.

[36] Herzlinger RA, Krandall SR, Vaughn HG. Neonatal seizures associated with narcotic withdrawal. J Pediatr 91:638-41, 1977.

[37] Tibbles JAR. Dominant benign neonatal seizures. Dev Med Child Neurol 22:664-67, 1980.

[38] Zonana J, Silvey K, Strimling B. Familial neonatal and infantile seizures. Am J Med Genetics 18:455-59, 1984.

[39] Pryor DS, Don N, Macourt DC. Fifth day fits: a syndrome of neonatal convulsions. Arch Dis Child 56:753-58, 1981.

[40] Goldberg JH, Sheehy EM. Fifth day fits: an acute zinc deficiency syndrome? Arch Dis Child 57:633-35, 1982.

41 Rowe JC, Holmes GL, Hafford J et al. Prognostic value of the electroencephalogram in term and preterm infants following neonatal seizures. Electroencephalography and Clin Neurophysiol 60:183-96, 1985.

42 Tharp BR, Cuhier F, Monod M. The prognostic value of the electroencephalogram in premature infants. Electroencephalography and Clin Neurophysiol 51:219-36, 1981.

43 Marshall R, Sheehan M, Escobedo M et al. Seizures in a neonatal intensive care unit: a prospective study. Pediatr Res 10:450, 1976.

44 Mellits ED, Holden KR, Freeman JM. Neonatal seizures II. A multivariate analysis of factors associated with outcome. Pediatrics 70:177-85, 1982.

45 Lou HC, Friis-Hansen B. Arterial blood pressure elevations during motor activity and epileptic seizures in the newborn. Acta Pediatr Scand 68:803-06, 1979.

46 Perlman JM, Volpe JJ. Seizures in the preterm infant: effects on cerebral blood flow velocity, intracranial pressure, and arterial pressure. J Pediatr 102:288-93, 1983.

47 Perlman JM, Herscovitch P, Kreusser KL et al. Positron emission tomography in the newborn; effect of neonatal seizure on regional cerebral blood flow in an asphyxiated infant. Neurology 35:244-47, 1985.

48 Younkin D, Maris J, Donlon E et al. The effect of seizures on cerebral metabolites in children. Pediatr Res 19:397A, 1985.

49 Diaz J, Schain RJ. Phenobarbital: effects of long-term administration on behavior and brains of artifically reared rats. Science 199:90-91, 1978.

50 Swaiman KF, Neale EA, Schrier BK et al. Toxic effects of phenytoin on developing cortical neurons in culture. Ann Neurol 13:48-52, 1983.

51 Freeman JM, Neonatal seizures. In Dreifuss FE, ed. Pediatric Epileptology. Boston, John Wright-PSG Inc. 159-72, 1983.

52 Painter MJ, Pippenger C, MacDonald H et al. Phenobarbital and diphenylhydantion levels in neonatal seizures. J Pediatr 92:315-19, 1978.

53 Donn SM, Grasela TH, Goldstein GW. Safety of a higher loading dose of phenobarbital in the term newborn. Pediatrics 75:1061-64, 1985.

54 Dodson WE. Antiepileptic drug utilization in pediatric patients. Epilepsia 25(suppl)2:S132-39, 1984.

55 Powell C, Painter MJ, Pippernger CE. Primidone therapy in refractory neonatal seizures. J Pediatr 105:651-54, 1984.

56 Deshmukh A, Wittert W, Schnitzler E et al. Lorazepam in the treatment of refractory neonatal seizures. Am J Dis Child 140:1042-44, 1986.

58 Koren G, Butt W, Rajchgot P et al. Intravenous paraldehyde for seizure control in newborn infants. Neurology 36:108-11, 1986.

58 Gamstorp I, Sedin G. Neonatal convulsions treated with continuous intravenous infusion of diazepam. Upsala J Med 87:143-49, 1982.

59 Gal P, Sharpless MK, Boer HR. Outcome in neonates with seizures: are chronic anticonvulsants necessary? Ann Neurol 15:610-11, 1984.

Department of Pediatrics
University of Connecticut Health Center
Farmington, CT 06032

Presenting...

VALUEplus

A new single premium variable life policy that offers investment opportunity through a choice of ***five*** popular options including zero coupon bonds—and guaranteed lifetime insurance protection.

PLUS...

- 100% tax-free asset accumulation
- Flexibility to move your investment as your needs or market conditions change
- Ready access to your funds
- Income tax-free transfer to heirs

ValuePlus offers you a way to plan for your own financial future and the future security of your heirs. It also provides the potential for substantial growth based on the performance of the funds you select. And...because ValuePlus is life insurance...***your investment grows on a tax-free basis.***

For a prospectus on ValuePlus containing more complete information, including all charges and expenses, mail the coupon below or call (phone number).

ValuePlus is issued by The Guardian Insurance & Annuity Company and distributed by Guardian Investor Services Corporation, both wholly owned subsidiaries of The Guardian Life Insurance Company of America

MAIL TO: **William C. Martin**
Second Vice President

Shearson Lehman Brothers Inc.
180 Westminster Mall, 2nd Fl.
Providence, RI 02903

401 272 1160
1 800 556 7362 Toll Free #

☐ Please send me additional information and a prospectus on ValuePlus. I'll read the prospectus carefully before I invest.

Name

Address

City State Zip

( ) ( )

Business Phone Home Phone

PRESIDENTIAL ADDRESS

Peter D. T. Clarisse, MD

I should like first to express my gratitude to the members of the Executive Committee and Council for their support during my term in office. I want to particularly single out our President-Elect, Richard Bertini, and our Immediate Past-President, Herbert Rakatansky, for their advice and support during these past twelve months.

I also wish to thank Dr. Norman Baxter and his executive staff who have been tireless in their efforts. In particular, I think the efforts of Dr Newell Warde of the staff should be commended. He is in charge of developing our computer capabilities, he helps draft speeches, he prints and publishes our newsletter, *Checkup,* he is in charge of keeping up with the legislature, and he provides administrative support for numerous committees. It is people such as these who make the Medical Society work. It is impossible to do without them.

This has been a year of growth for the Society. It has been an exciting year. A year of significant change. As a Society, we have made significant progress in our efforts to become a more proactive organization.

Delivered at the Annual Meeting of the Rhode Island Medical Society, May 15, 1987.

One of our very first actions last year was to obtain an AMA Management Study to see how we could improve ourselves and become more effective. This study's number one recommendation was that the Society engage in systematic long-range planning, and it recommended that the Council be the long-range planning committee.

As a consequence, again with the help of the AMA, the Council sat down with Bruce Balfe, AMA Vice President for Issues, Planning, and Management, to hammer out goals and priorities. It was not an easy task. It took two full days for us to develop a general outline. However, we agreed that any priorities we set had to take into account three factors:

1. The services we provide have to be essential to the needs of doctors today.
3. The services we provide are not substantially duplicated by other organizations.
3. The Medical Society must have the resources (both financial and administrative) to perform those services felt to be priorities in a consistent and high quality manner.

Using these guidelines, it quickly became apparent when listing needs and priorities, that the Society's role today is no longer one of disseminating scientific information. Most of us get our

scientific information from other sources.

Therefore, it was obvious to the Council that our Library — which takes up a significant portion of this building — was no longer of material benefit to the Society or its doctors. Its use had declined to the point that we could no longer keep a librarian. Due to its extensive collection of journals and rare books, there had been reluctance in the past to dispose of it.

However, the needs of our doctors today demand that we make the best possible use of our available resources. The Library was underutilized. Its services were extensively duplicated by other organizations. The Library had become a resource that we could no longer justify.

Removing the Library was not an easy step, but it was necessary. It will be of great benefit to the Society in the future. As you all know, we received an extremely attractive offer from Brown University which the Executive Committee, the Council, and the House of Delegates have accepted. As a consequence, the Library will be moving to Brown University, where the rare-book collection will be properly housed and displayed. The agreement also stipulates that the rare-book collection will remain intact and never be sold. Rhode Island Medical Society members will now have full access, without cost, to all the Brown University libraries in perpetuity. This is a major benefit that we have never had before.

The Council has also taken steps to alleviate one of our major perceived weaknesses — effective communication. The first step was to address the lack of immediacy in the *Rhode Island Medical Journal* — it took six weeks to publish. As a result, the information in the newsletter section was often dated. A new vehicle for communicating with the members was necessary.

We now have a separate newsletter, *Checkup,* which is published in the Society's offices, and has a turnaround time of four to five days. *Checkup* allows us to provide accurate and important information on a timely basis. We can also provide special issues, such as the one on AIDS and tort reform. We intend to build on this newsletter, to extend it, and to improve it.

The Executive Committee and Council have authorized the Society to upgrade its computer capability, so that we can fully be integrated with the AMA's data bases. This will enable us to have much more information available on both the local and national levels. It will allow us to get this national information to our members much more quickly and easily. This upgrading is currently taking place and should be fully functional within the next several months.

The Society has recently become involved with the state Department of Elderly Affairs (DEA). We have developed a voluntary medicare assignment program for individuals who are enrolled in the Rhode Island Pharmaceutical Assistance to the Elderly Program. All low-income elderly Medicare patients will be able to receive doctors' services at discounted rates.

This program and our involvement with the DEA have opened another avenue for the Society. I have been on several television and radio talk shows with a representative of the DEA to discuss this program. This exposure has brought the Society to the community, and it has let them know that we are concerned about the costs of medical care. Although we don't know at this time the outcome of the current state bills on mandatory assignment of fees under Medicare, it is very obvious that without a program of this sort, mandatory assignment would be voted by the legislature with very little hesitation.

Lastly, as you all know, the Society has participated over the past year in two coalitions on tort reform. One was the Governor's Blue Ribbon Commission and the other, the Tort Reform Coalition headed by the Chamber of Commerce. The recommendations of both groups amount to significant change in Tort law and are now before the General Assembly. How many of the recommendations become law is anybody's guess. However, one thing is certain, if we do not continually press our legislators for reform, nothing will happen. That means we have to maintain an active and visible presence on the hill. What's ahead for us?

The process of long-range planning, which we have begun this year, is one that will continue forever. Our focus may shift from year to year as we complete projects, but it will go on. As you can imagine, despite Rhode Island's small size, we still have to do all of the things a larger State Medical Society has to do — but we have to do them with a smaller number of members.

Revenue remains a problem. We need adequate resources to be effective for you. Disposing of the Library will stop a drain on those resources, but it will not enhance our financial base. As a consequence, we have started looking into alternatives for the space being made by the removal of the Library. Our plan is to turn this space into useable income-generating real estate.

We must increase our visibility at the legislature. We now have two lobbyists — one who is up there all the time — and one who works be-

hind the scenes. They are not substitutes for us. RIMS members must continue their legislative effort. The liability problem has not gone away. We must continue to make ourselves heard, to work with others in order to bring about reform, to make sure that we participate in, and help to formulate changes that affect the health of our citizens.

One of the most important ways to increase our effectiveness for doctors is to have a fiscally sound and active political action committee (RIMPAC). All of us by now must see how important the legislative arena is to us. We need to get that message to our members. The Society may wish to consider voluntary assessments to RIMPAC. The time has long passed when doctors can claim to be apolitical because politics does not interest or affect them. The facts of the matter are that politics is necessary, most politicians are honest, and all of them want to hear from us. A lack of communication with our legislators is not a tenable position and is most detrimental to the future of health care.

In the media age we must continue to train ourselves to communicate more effectively and understandably with other people. Duffy and Shanley, our public relations counsel, has helped us make significant strides in this regard. As we become more expert ourselves, we hope to take over some of these duties, but this effort must continue. It must expand.

I remain confident in the future of organized medicine. However, we can only be confident if we remain responsive to the change around us and if we help manage that change, not let it manage us. We have to adapt to new situations with new ideas and effective solutions. I believe that we have demonstrated this past year that we can adapt to those changes.

I feel proud to have been your President for the past year, and I want to thank all of you for your support and cooperation. I know you will extend that same support to your new officers.

There must be a good reason why

UNITED SURGICAL CENTERS

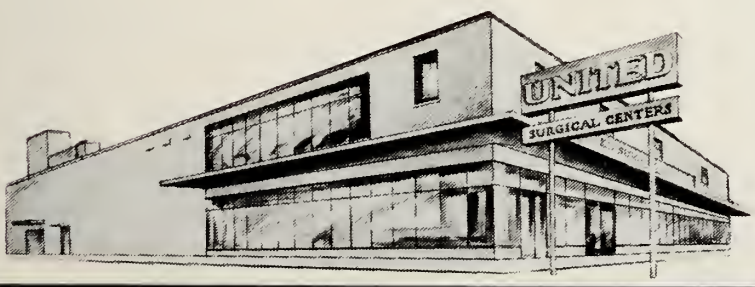
The Professionals in Home Health Care Equipment

we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.



(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

There are three ways to bill

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
NS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	HARGE	CREDITS Payments	CREDITS Adj.	URRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85		Medicare pmt/adj.		-45.-	-8.-	47.-
10/10/85		Patient pmt.		-7.-		40.-
10/25/85		Medicare pmt/adj.		-28.-	-5.-	7.-
11/10/85		Pt pmt.		-7.-		-0-
11/20/85	James	Int. O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	800.-	Billed 12/20/85		840.-
1/5/86		Medicare pmt/Adj		-28.-	-5.-	807.-
1/17/86		Court. adj.			-3.-	804.-
2/2/86		Medicare pmt/Adj		440.-	250.-	114.-

PLEASE PAY A[illegible] AM[illegible] N[illegible] TH[illegible] O[illegible] MN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	DSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit			RPT	Report
CS	Cash	NJ	Injection	S	Surgery

[illegible] DPT [illegible] OR AC[illegible] N[illegible] APPEARS ON YOUR RECEIPT ARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

AMOUNT REMITTED

James Smith
100 Main Street
Any City, USA

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

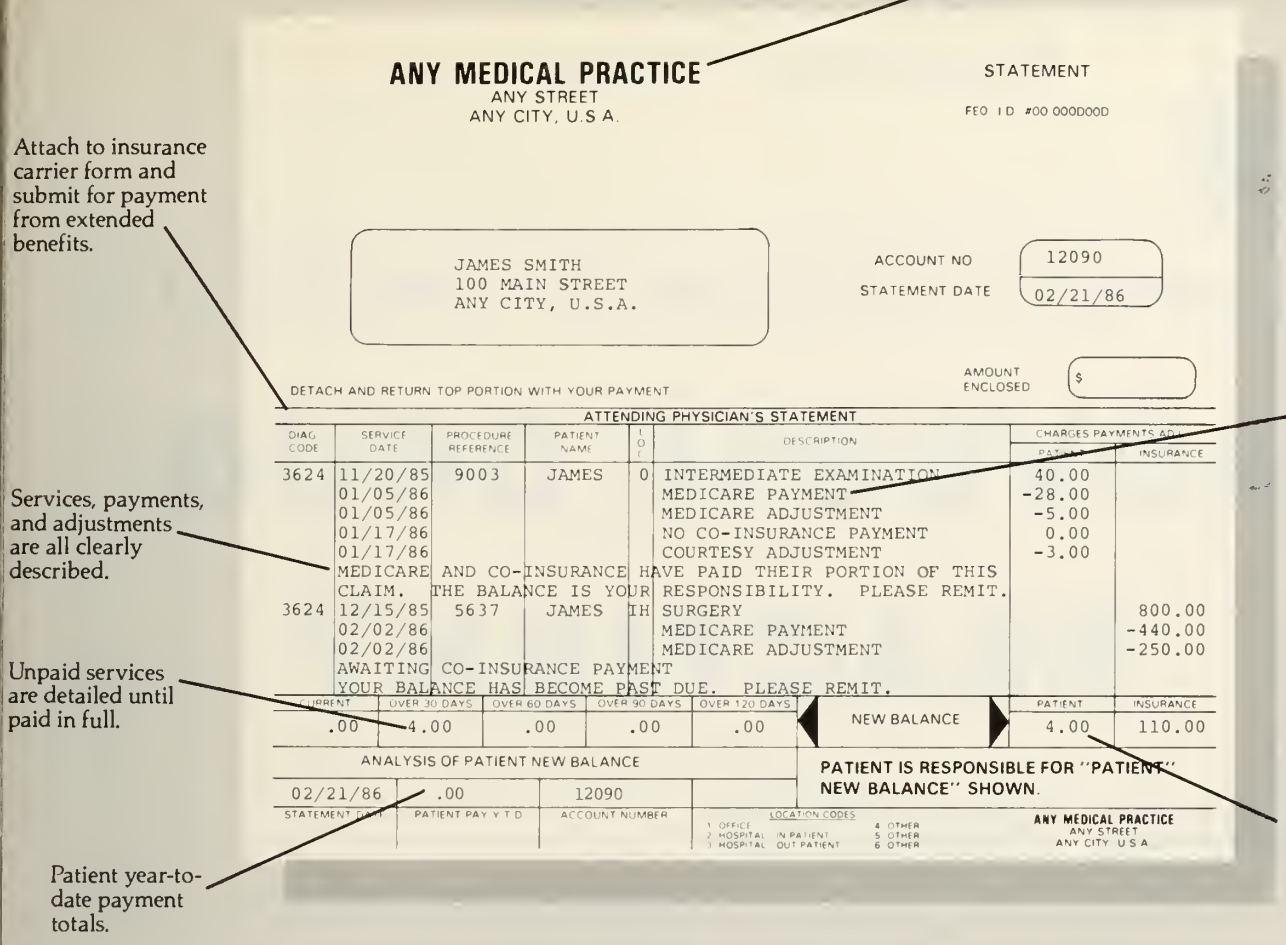
BILLED FROM 1-21-86
BILLED TO 2-20-86
DATE 2/21/86
ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

your patients.



THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

Rhode Island

ADVERSE DRUG REACTION Reporting Project

SUSPECT A SERIOUS OR UNEXPECTED

ADVERSE DRUG REACTION?

Please Report It.

SUSPECTED ADVERSE REACTION REPORT (For All Drugs and Biologics)

IMPORTANT: SUBMISSION OF A REPORT DOES NOT NECESSARILY CONSTITUTE AN ADMISSION THAT THE DRUG CAUSED THE ADVERSE REACTION

PATIENT INITIALS (Optional)	AGE (Years)	SEX	DATE OF REACTION ONSET
A.D.R.	54	[/] MALE [ ] FEMALE	12 Oct. 1986

DESCRIBE REACTION(S) (Give signs, symptoms, diagnoses, course and lab findings)

JAUNDICE

CHECK ALL APPROPRIATE TO REACTION
- [ ] DIED
- [/] TREATED WITH Rx DRUG
- [/] INPATIENT HOSPITALIZATION
- [ ] SEVERE OR PERMANENT DISABILITY
- [ ] EMERGENCY ROOM TREATMENT
- [ ] TREATMENT IN PHYSICIAN OFFICE
- [ ] NONE OF THE ABOVE

SUSPECTED DRUG(S) (Trade Name is preferred. If a generic product, give manufacturer. Indicate Lot No. for vaccines, biologics)

[redacted]

REASON FOR USE OF DRUG(S)	ROUTE	TOTAL DAILY DOSE	DATES OF ADMINISTRATION
HYPERTENSION	P.O.	100mg.	9 Sept.- 12 Oct. '86

OTHER DRUGS TAKEN CONCOMITANTLY (Exclude those used to treat reaction)
None

OTHER RELEVANT HISTORY (e.g., Concomitant Diagnoses, Pregnancy, etc.)
None

PHYSICIAN NAME AND TELEPHONE NUMBER
J. Doe, M.D. 277-2550

Confidential

ALSO REPORTED TO MANUFACTURER [/] YES [ ] NO

For report forms, guidelines and information contact S. Rosenbaum, PhD, 277-2901

A pilot project of the Rhode Island Department of Health
sponsored by the U.S. Food and Drug Administration

During this the 175th Anniversary year of the establishment of the Rhode Island Medical Society we shall publish from time to time papers of historical interest relevant to Rhode Island. Doctor Waterhouse (1754-1846), who was Professor of the Theory and Practice of Physic at Harvard Medical School, was a native of Newport, Rhode Island.

Cautions to young persons concerning health

in a

PUBLIC LECTURE

delivered

at the close of the MEDICAL COURSE

in the

CHAPEL *at* CAMBRIDGE

Nov. 20, 1804;

containing

the GENERAL DOCTRINE of CHRONIC DISEASES;

shewing

the EVIL TENDENCY of

the USE of TOBACCO upon

YOUNG PERSONS;

more especially

the PERNICIOUS EFFECTS of SMOKING CIGARRS;

with observations on

the USE of ARDENT and VINOUS SPIRITS in general

BY BENJAMIN WATERHOUSE, MD

PROFESSOR OF THE THEORY AND PRACTICE OF PHYSIC, AND TEACHER OF NATURAL HISTORY IN THE UNIVERSITY OF CAMBRIDGE.

—ut sit mens sana in corpore sano.
JUV.

Printed at the UNIVERSITY PRESS by W. Hilliard.
MDCCCV.

TO THE MEDICAL STUDENTS, RESIDENT GRADUATES, AND SCHOLARS OF EVERY CLASS.

YOUR application for a copy of my lecture for the press indicates a disposition to persevere in the general resolution, to relinquish an unhealthy and unseemly practice.

I shall set a value on this production, should I hereafter find, that it has in any way assisted you in the attainment of that greatest of all earthly blessings, "A SOUND MIND IN A SOUND BODY."

BENJAMIN WATERHOUSE.

Cambridge January 1805.

GENTLEMEN,

During the first three or four years of our medical establishment I frequently found it needful to give public lectures in this place. Even eight or ten years after its establishment it was customary to commence and to close the medical course by a public lecture in the chapel.[1] The custom however has been discontinued several years, as nothing special excited a wish to address you altogether. Whether its revival at this time, be for a trivial or beneficial purpose, you yourselves will judge.

When our venerable forefathers fixed upon this spot, as a fit place for the education of youth, they doubtless had regard to the health of its inhabitants. A gravelly plain, near the banks of a tide river, and in the proximity of the sea, together with good springs of pellucid water,[2] must have led our sagacious ancestors to conclude, that this was a salubrious spot for a college. Time has done honour to their judgment, as during one hundred and fifty years the town of Cambridge and the College have exhibited a succession of joyful instances of juvenile vigour, healthy manhood, and comfortable old age. From observations, made by the late excellent Dr. Wigglesworth,[3] it appears, that there occurred fewer, much fewer deaths, among the collegians, than among any set of young men in any part of the Commonwealth. Since my connexion with this University as Professor, I can bear testimony to the healthiness of the inhabitants of the town in general, and of the students in particular.[4] I have noticed the young men within these walls with pleasure, as a blooming, cheerful, hungry assemblage of youthful activity. But does this charming picture any longer exist? Is it not faded and fading, like a flower, that has passed its bloom; and which is about to wither on its stalk? If this idea be just, surely the *cause* of this faded aspect in the plants of our Seminary calls loudly and affectionately for investigation. If the full bloom of exuberant health once marked and adorned these seats, and this bloom is fled, or fleeing away; it is certainly an object of prime importance to inquire, *whence this DETERIORATION?* Were I not persuaded that it might be traced to a moral as well as a physical source I would not have appeared at this time before you. My motive is your welfare and the happiness of your parents; for what are riches and knowledge without health to enjoy them? But alas! the young, the gay, and the giddy abuse health through ignorance; and when better informed, some of them refuse to stop, or lend a listening ear to the warning voice of Nature and common sense; while *"he that taketh heed prolongeth his life."*

It is proper to inform you, that we are led in the order of instruction to speak, at this period of our course, *of those disorders, which mankind* BRING UPON THEMSELVES BY THEIR OWN IMPRUDENCE.

It was a sagacious saying of one of the antients, that "GOD *sends* ACUTE *diseases, but* CHRONIC *disorders we create ourselves."*

ACUTE diseases are such, as proceed with rapidity, and terminate soon; such are violent fevers, plurisies, quincies, and epidemical disorders. They are generally owing to a cause, that "walketh in darkness," being such as prudence could not obviate, nor our prescience guard against. The superstitious are apt to ascribe the most dismal diseases and most shocking accidents to the anger of invisible beings; thus when the plague was desolating the Grecian camp, instead of resorting to human remedies, they had recourse, like our Indians, to incantations and inchantments.

CHRONIC diseases are those, that come on slowly, and continue long. We place under this head *depraved appetite, jaundice,*[5] and the long and gloomy train of *nervous disorders.* To these we may add *gout, asthma,*[6] *palsy,* and *apoplexy;* as well, as that imbecility or morbid derangement of the absorbent system, occasioning *dropsies;* which is accompanied by that generally depraved habit of body, known among physicians by the name of *cachexia;* all of which are owing to *chronic weakness;* the source of which is an imbecility of the digestive organs, occasioning errors in "the first concoction," which deranges the whole chain of processes, occurring between chylification and sanguification.

Perfect health requires the temperate action of

the vital influence through every part of the system. In perfect health food is sought with appetite, enjoyed with relish, and digested with facility. In perfect health every secretion and excretion is duly performed. Perspiration is neither deficient nor excessive. The breathing is free and easy, requiring neither conscious exertion, nor even a thought. The action of the heart and arteries with the consequent circulation of the blood is regular and placid; neither too rapid nor too indolent; neither laboured nor oppressed. In perfect health the body continues in the exercise of its proper functions without the least sensation of difficulty or embarrassment. The mind undisturbed by any violent emotions, agitations, or depressions of a corporeal nature, is in a state for exercising its noblest powers and tranquil vigour. The body is perfectly free from pain, oppression, hebetude, and every species of uneasiness; and a certain vivacity, not to be described, reigns throughout the system.[7] This happy, but evanescent condition, constitutes the *"mens sana in corpore sano"* of Juvenal, *"a healthy body and a mind at ease."*

The first derangement of this delightful state is felt in the stomach. Its faculty of communicating impressions, made by various substances taken into it is such, that it seems more like a nervous expansion from the brain, than a mere receptacle for digesting food. We shall speak of this faculty hereafter; and confine our view at present to the function of digestion.

Digestion is the selection and conversion of some foreign pabulum or food into our own nature. There are within us two organs, performing at the same time two different kinds of digestion; for while the stomach is digesting *solid substances,* the lungs are digesting *air.*[8] Digestion of solid substances by the stomach is the conversion of food into chyle, and of chyle into blood. A regular supply of this milky fluid is necessary to recruit and repair those parts of the animal machine, that are incessantly wearing down, and passing off, by the very actions requisite to life. When this function is impaired and much deranged, the patient languishes, becomes emaciated, faints, and at length dies. If digestion be well performed, that is completed within three or four hours,[9] the chyle is proper, be the food ever so various. Blood formed from this chyle is natural; the secretions and excretions are regular; and health, strength, activity, and cheerfulness ensue. But if digestion languish, the contrary of this will happen, be the food whatever it may.

That the Lungs *digest* air may be to you a novel doctrine. These vital organs are made up almost entirely of two sets of vessels, one conveying air, the other blood. When we inhale atmospheric air, these organs in the action of breathing separate a portion of that inspired mass, called *oxygen* or *vital air,*[10] which entering the blood vivifies and animates the whole frame; and actually becomes one of the constituent principles of our bodies. Between this *oxygenation* of the blood through the lungs, and the digestion of the food by the stomach there exists an inseparable sympathy and a beautiful balance. When we breathe the oxygenated air of the mountains or of the open ocean, we feel not merely a keener appetite, but a greater quantity of food than ordinary will be digested without oppression of the stomach, or labour of the lungs. In fewer words, it is oxygenation, that excites the dormant energies of the brain and nervous system, which invigorates every fibre, giving strength for debility, and activity for sluggishness.[11] Such is the conspiration of action between the stomach and the lungs, and such the sympathy of both with the whole human system, that these organs are either primarily or secondarily affected by every malady, that flesh is heir to.

The first intimation of a chronic disorder is almost always felt in the stomach. That wonderful organ has a remarkable contractility, by which it applies the inner surface closely to the materials it incloses.[12] That distressing sensation, called *"a sinking"* at the stomach, is owing to a diminution of its power of contraction. The healthy contractility of this prime organ of digestion is not owing merely to the force of its own fibers, but depends on the joint energy of the whole system, corporal, and corporeal; for the more vigorously the stomach applies itself to its contents, the more speedily is digestion performed, and the braver does a man feel, the better does he walk, think, and write.

The disorder progressing, the patient is oppressed with listlessness and sense of weight over all his body; he becomes pale at certain intervals, and a sweat breaks out, irregularly in different parts of his body. Digestion is slow in consequence of which the patient is distressed with mawkishness, sourness, heartburn, and nausea, with frequent calls for food, from a sense of *sinking,* not from genuine hunger. The distention of the alimentary canal by flatulency increases the distress of the sufferer. It is remarkable, that in this state of the stomach, wine is more eagerly desired, than at any other time.

The causes of the disorder continuing to be applied, sleep is disturbed and followed by torpor, bordering on stupidity; the patients eyes become hollow and lose their vivacity; a universal debility most sensibly felt in the digestive organs, with an encreased or morbid irritability, perverting their regular actions the pulse is quickened, the breath labours, cough comes on, and consumption follows.

When the fountain of health is thus disturbed, the smallest streams must also be deranged. Can we wonder then, that the *ultime vasculae* and the *minimae fibrillae* of the organ of intellect are finally affected, occasioning despondency of mind; or else peevishness, doubts, fears, wandering thoughts, and ridiculous fancies? The disease seldom proceeds to this in very young persons.[13] As imprudence in youth lays a foundation for *Hypochondriasis* in certain temperaments in manhood, you cannot be too cautious of the first breaches on your tender constitutions. If in youth you transgress the first principles of nature, She may punish you in future life with a long and dismal train of NERVOUS DISORDERS, than which there cannot be a greater torment. A *nervous* man may escape volcanic eruptions, earthquakes, hurricanes, inundations, mobs, sieges, and revolutions; but whither shall he fly to avoid heats and frosts, a lowering sky, and east winds? To what city or village shall he repair, that is not infested with creaking doors, jarring windows, screaming children, and fretful inmates, to lacerate his *nerves,* and render him the most wretched being under heaven!

Having given you a description of cheerful health and of its deviation into gloomy disease, let us now see if we cannot discern some general cause or causes, producing this declension.[14]

Moral philosophers unite with physicians of the first rank in opinion, that all chronic disorders arise from either 1st. VEXATION OF MIND, or 2d. an INDOLENT AND SEDENTARY LIFE, or 3d. INTEMPERANCE; or from the cooperation of any two of them; or from the combination of all three.[15]

It is a melancholy reflection, that there are as many pressed down to the grave by chronic disorders, brought on by a troubled mind, as are cut off by acute ones. Envy, jealousy, concealed resentment, and the corroding discontents of a life of penury and neglect, have slow but destructive effects on the delicate mind and "fine spun frame." A man is often cheerful under the loss of a limb; and long habit may render a deranged state of health tolerable; *"but a wounded spirit who can bear?"*

The first effect of violent grief or trouble of mind is deprivation of the powers of digestion. A man in the best health, the highest good humour and spirits, as well as good stomach, sitting down to dinner with his friends, receives suddenly some very afflicting news. Instantly his appetite is gone, and he cannot swallow a morsel. Let the same thing happen after he has made a hearty, cheerful meal, as suddenly the action of his stomach ceases, the whole power of digestion is cut off totally, as if it were become paralytic; and what he has eaten lies a most oppressive load. Now what connexion is there between a piece of bad news and a man's stomach, full or empty? It is, says *Cadogan,* because the animal spirits or action of the nerves, whatever be the secret cause of their power, are called off to supply and support the tumultous agitation of the brain, and the stomach with all its appendages and secretions is left powerless and paralytic. In this case the lungs, which always sympathize with the distresses of the stomach, endeavour to relieve their oppression by a deep sigh.

The principle agent in the process of digestion is a peculiar fluid, secreted in the stomach, called the *gastric juice.* The quantity and activity of this singular liquor depend on the contractile power of the digestive organ, as a proximate cause; and on the energy of the whole system, as a remote one. In silent, long continued grief this fluid is deficient in quantity and depraved in quality. The chyle is of course vitiated and the functions of the stomach perverted; its contents become sour, bitter, and rancid. The sufferer pines away for want of a nourishing supply; an universal bad habit of body ensues; a complication of disorders, succeeding each other always from bad to worse; and unless the wretched person can subdue anxiety, he sinks under his misery, and dies, as is said, of a broken heart.[16]

In turning away from this sorrowful picture, I wish you to remember, that it is *the stomach which first suffers;* and that whatever damps the spirit, injures that organ; and we shall see hereafter, that whatever injures the stomach, depresses the spirits.

Let us now advert to causes more common and more applicable to the main object of this lecture.

The causes of *Dyspepsia*[17] or bad digestion, the grand inlet to all chronic disorders, arrange themselves under *two* heads. First those, which act upon THE WHOLE BODY, or particular parts of it, but in consequence of which the *stom-*

ach is chiefly affected. Secondly those, which act *directly* and *immediately* upon the STOMACH itself.[18] To these we may add a third, viz. causes, which act at the same time upon *both*.

An *indolent* and *sedentary life* we place at the head of causes, which act upon the whole body; next to this

Trouble of mind, of which we have already spoken: and lastly

A rakish life.

Need we go far for arguments to prove, that the only rational creature on earth was destined to exercise and improve the faculties of his mind as well, as the powers of his body. The PARENT OF UNIVERSAL NATURE has imposed, kindly imposed on his children, the salutary task of moderate labour, as the best means of preserving their health and their innocence. He has in like manner encouraged them to exercise the towering faculties of their minds by the contemplation of His works; and has given them a thirst after useful science, stimulating them to amend their natural condition. He has accordingly decreed, that the prudent exercise of the corporal and mental powers should strengthen each other. To live a live of indolence is to sin against one of the first laws of our Creator; accordingly we find, that the offender is punished with loss of health and spirits.

The time, alloted to a lecture, is not sufficient to go into a description of the subtle operations of the body. We may remark generally, that our best health, strength, and spirits, depend on the good and natural state of the minutest and almost imperceptible vessels and nerves of the body. The little diminutive pipes and tubes, the extended continuations of larger vessels, must be kept free and open. I consider the body, says *Addison*, as a system of tubes and glands, or a bundle of pipes and strainers, fitted to one another after so wonderful a manner, as to make a proper engine for the soul to work with.[19] The strength of the heart and arteries alone in a sedentary life is by no means sufficient to keep up and perpetuate the requisite motion of the fluids through these capilliary vessels; but it requires the assistance and joint force of all the muscles of the body to propel and accelerate the circulation of the whole mass of blood, in order to keep these minute tubes pervious and clear.[20]

That sprightly vigour and alacrity of health, says *Cadogan*, which we feel and enjoy in an active course of life, that zest in appetite and refreshment after eating, which sated luxury seeks in vain from art, is owing wholly to *new blood, made every day from fresh food, prepared and distributed by the joint action of all parts of the body*. No man, says he, can have these delightful sensations, who *lives two days with the same blood*. To introduce new juices, the *old* must be thrown off; or there will be no room, there will be too great a plethora of fulness. In a state of indolence or inactivity the old humours pass off so slowly, the insensible perspiration is so inconsiderable, that there is no void to be filled; consequently by degrees the *appetite* or *desire of supply* must daily diminish, and at last be totally lost.[21] To this doctrine morbid indolence will reply, that this plethoric or crowded state of the system with all the disagreeable feelings, consequent thereon, may be removed by evacuating medicines. There is no reasoning with those, who had rather take a purge, than a walk; or an emetic, than a ride.

Some of you injure your health by too close application to study. Sedentary thoughtfulness will wear out the body, and generate diseases that shorten life. A dyspeptic stomach, emaciated body, and irritable feelings, compose the heavy tax, which men of fine intellects and deep study pay for their eminence. But there is a sort of *lazy literature*, a kind of *suspended animation*, which engenders many chronic diseases, that embitter and shorten life. This torpid state, in which mind and body are equally stagnant, occasions tasteless meals, perpetual languor, and causeless anxiety. Here the body is not *worn*, but *rusts* out. In this state, wine, ardent spirits, and tobacco are eagerly coveted.

Let us next consider impressions made *directly* and *immediately* on the stomach.[22]

To remove the sinking, dismal languor and dejection, brought on by offending against the first principles of our nature, men turn for a momentary relief to

INTEMPERANCE:

Which is commonly an application of stimulating and narcotic things to the stomach. But who shall define *Temperance?* a work like liberty, different in signification in different countries. Before you can adjust the criterion of temperance, you should visit some of the colleges on the continent of Europe, where a piece of bread, an egg, or an onion with a draught of milk and water, is thought a tolerable meal. There is however an absolute, determined temperance, measured by every man's unprovoked appetite and consumption; a mean, at which virtue takes her stand.

If a man go on daily taking more than he needs or can get rid of, he feels oppressed, his appetite fails, and his spirits sink. Then he has recourse

to rich, stimulating food; and though he washes down each mouthful with a glass of wine, he can relish nothing. Thus distressed, he applies to the Doctor *to give him an appetite!* who, after evacuating him upwards and downwards, gives him *aromatic bitters* infused in *wine* or *brandy, elixir of vitriol;*[23] *bark, oil of wormwood, steel, columbo, soap, aloes,* and *rhubarb; quassia* and *limewater.* Some of these by giving contractility[24] to the imbecile organ afford a short respite to his sufferings. They may moreover effect a transient but fallacious relief by forcing the concocting powers to squeeze their crude austere contents into the blood; until at length oppressed, Nature resents the injury in the form of *gout, palsy,* or *apoplexy.* A skillful, honest physician, will say in such cases, — your cure can only be found in EXERCISE. A ride with the cheerful scenery of a new and beautiful country will give you health, vigour, and vivacity, sound sleep, and a keen appetite. But no drugs can act upon your blood and juices, like the joint force of all the muscles of your body, acting and reacting, as in a regular course of moderate exercise; nor can any of our draughts and portions *oxygenate* your pulmonic blood, like the inspiration of the salutiferous air of the mountains.

"The first physicians by debauch were made.
Excess began, and sloth sustains the trade.
By chace our longliv'd fathers earn'd their food;
Toil strung the nerves, and purify'd the blood.
But we their sons, a pamper'd race of men,
Are dwindled down to three score years and ten.
Better to hunt in fields for health unbought,
Than fee the Doctor for a nauseous draught.
The wise for cure on exercise depend:
GOD never made his work for man to mend."
Dryden.

We have said,[25] that the causes producing chronic diseases, arranged themselves under two general heads; — those, which act on the *whole body,* and which affect the stomach in a *secondary* way; — and those, which act *directly* on the stomach, and affect the whole body through the medium of that organ; that to these we might add causes, acting upon the *whole body* and *upon the stomach* at the same time; such for example as

A RAKISH LIFE. A rakish life is too well known to need a description. It is often a *halo* of misery, surrounding the brightest genius! To point out its ill effects would be an insult to your understandings. I might as well labour to convince you of the blessings of health or the advantages of industry. I pass the subject over in silence, only remarking in the words of Martial, "*Balnea, Vina* VENUS[26] consumunt corpora nostra."

Instances of young gentlemen sinking deep into the scandalous habit of drinking ardent spirits are very rare indeed; yet it would not be difficult to prove, that there is and has been for several years six times as much ardent spirit expended annually here, as in the days of your grandfathers. Unruly wine and ardent spirits have supplanted sober cider.[27] Is it not the case, that some use them of that strength and in that quantity, which is not consistent with the regular functions of the brain?[28] Many, warmed by the generosity of youth, may think it consonant with prudence to drink so, as to produce that exhilaration of spirits, which takes place just on this side intoxication; but I hesitate not to pronounce, that the repetition of such practices is pernicious to health and dangerous to morals. Cannot wisdom devise a plan of social intercourse, independent of the stimulus of the bottle? It is said such plans existed in the city of GENEVA, before the French inflicted the benefits of their liberty on that philosophic people.

Among the causes, which act directly and immediately on the stomach, we mentioned, besides ardent and vinous spirits, certain NARCOTIC substances.

NARCOTICS are soporiferous drugs, which induce stupefaction. It is the property of narcotics to exhilarate first, and then to relax and stupify. They invariably debilitate the organs, to which they are *immediately* applied; at length they have a similar effect on the whole system. At the head of this class of drugs we place OPIUM,[29] which is the milky juice that exudes from the heads of poppies, when incisions are made in them; and then gradually dried in the sun. To this class belong also *Cicuta* or hemlock, *Belladonna* or deadly nightshade, *Stramonium* or apple of Peru, and NICOTIANA or *Tobacco.*

The Turks, who were forbidden by Mahomet to drink wine, intoxicate themselves with opium. It is said, that some will eat more than an ounce in a day. We have seen, that nothing so effectually preserves health and prevents disease, as maintaining the tone and regular motions of the digestive organs; and there is no drug in common use, which renders them so torpid, and which so effectually stagnates their functions as opium. After destroying the energy of the stomach, it undermines the powers of all the other organs in succession, even to the organ of *thought.* Travellers inform us, that the visage and general ap-

pearance of the opium-eaters in Turkey are the most disgusting imaginable; even worse than our most abandoned rum-drinkers. Some of these miserable Turks have however mind enough left to destroy themselves by the dagger, to prevent living or rather *breathing* a few years longer in a state of confirmed idiotism, which is the fate of most of them during the latter years of their existence. Thus much for *opium:* — but what shall we say of *Nicotiana*[30] or our beloved TOBACCO?

With what caution should a man proceed in attacking a favourite of the people? A prudent man, one who wishes to sail quietly down the popular stream, would be disposed rather to flatter and applaud the object of their affections. But an honest man, who differs a little from him, commonly designated as a prudent one, can never flatter, where he feels a friendship. He will give the true character of a dangerous inmate, and warn his friend of the consequences of cherishing a viper in his bosom. You already perceive, that although we would give "fair play" even to a treacherous enemy, yet Tobacco has done and is secretly doing too much mischief to expect any more from us, than a severe trial and rigorous justice.

The great LINNAUS has beside his celebrated *artificial* classification given us a *natural* one. In his *natural* arrangement he has placed *Tobacco* in the class *Luridae;* which signifies pale, gastly, livid, dismal, and fatal. To the same ominous class belong Foxglove, Henbane, Deadly-nightshade, and another poisonous plant, bearing the tremendous name of *Atropa*, one of the Furies. Let us examine one of them, viz. TOBACCO, its qualities, and its effects on the human constitution.

When Tobacco is for the first time taken into the mouth, it creates nausea and extreme disgust. If swallowed it excites violent convulsions of the stomach and of the bowels, to eject the poison either upward or downward. If it be not very speedily and entirely ejected, it produces great anxiety, vertigo, faintness, and prostration of all the senses; and in many instances death has followed. The oil of this plant is one of the strongest of vegetable poisons, insomuch that we know of no animal, that can resist its mortal effects. These are, without exaggeration, some of the *lurid* qualities of our beloved tobacco. Let us now see, if it can be agreeable to the laws of the animal economy, or consonant to common sense, that a plant with such qualities can act otherwise than detrimental to the tender constitutions of young persons.

The human organs are endowed with a faculty of selecting certain wholesome articles, and our digestive apparatus of assimilating and changing them into our own nature and substance. Beside this nutritive faculty our organs are endowed with a repulsive one, with certain instincts or perceptions, by which they reject whatever is unwholesome or pernicious to our well being. These powers and faculties, purely instinctive, are more or less possessed by every *healthy* animal. Man endued with reason has these instincts in less perfection, than the brutes.

The organs of the senses are so many guards or centinels, placed at those avenues, where death is most likely to enter. For illustration let us suppose a man cast ashore on some uninhabited island, and roaming among unknown fruits and herbs with a desire to satisfy his hunger; he knows not whether, what he finds be wholesome or poisonous. What *naturally* follows? The first examination, which the vegetable undergoes, is that of the *eye;* if it incur its displeasure by looking disagreeable and forbidding, even this may induce him to throw it away; but if it be agreeable to the sense of seeing, it is next submitted to the examination of the *smell*, which not unfrequently discovers latent mischief concealed from the sight; if not displeasing to the sight, nor disagreeable to the smell, he readily submits it to the scrutiny of the next guard, the *tongue;* and if the taste too approbate the choice, he no longer hesitates, but eating it, conveys it into his stomach and intestines; both of which, like faithful body guards are endowed with a nice perception and prompt action, by which, if what was eaten as wholesome food, should notwithstanding all the former examinations still possess a latent quality, injurious to life, the stomach is stimulated to reject it upward, or the intestines to expel it downwards. These internal perceptions and consequent exertions are the first and most simple acts of nature, being purely instinctive, constituting what physicians call the *"Vis medicatrix nature,"* or reaction of the system.[31]

Let us suppose, that our hungry adventurer had fallen on the tobacco plant; he would find nothing forbidding in its appearance; to his smell it would be rather ungrateful; to his taste so nauseating, that it is surprising, how the same man ever ventured to taste green tobacco twice; but if taken into his stomach, convulsions, fainting, and a temporary loss of his senses follow; accompanied with violent and nasty operations. If that, which is wholesome, affect the senses of animals with pleasure, and invite them to convert it into their own juices; and if that, which is unwhole-

some, excite disgust in smell, taste, and appetite, then would our adventurer rank this herb among poisons, and note it as one of those, which nature forbade him to use. Yet man by perverting his nature has learnt to love it! and when perverted nature excites a desire, that appetite or desire is inordinate and ungovernable; for the reaction or physical resistance to evil will, like that of the moral, lessen in proportion to the repetition of the attacks; and then those guards of health, already mentioned, desert nature, and go over to the side of her enemy; and thus we see how intemperate drinking and immoderate smoking began their destructive career.

The first effect of tobacco on those, who have surmounted the natural abhorrence of it; and who have not only learnt to endure it, but even to love it; and who have already commenced the nasty custom of chewing or smoking, is either a waste or vitiation of the *saliva.*

The *saliva* or spittle is secreted by a complex glandular apparatus from the most refined arterial blood, and constantly distils into the mouth in health; and from the mouth into the stomach at the rate of twelve ounces a day.[32] It very much resembles the gastric juice in the stomach; and its importance in digestion may be imagined after listening to the words of the great BOERHAAVE. "Whenever the saliva is lavishly spit away, we remove one of the strongest causes of hunger and digestion. The chyle prepared without this fluid is depraved, and the blood is vitiated for want of it. I once tried," says this great philosopher and consummate physician, "an experiment on myself, by spitting out all my saliva; the consequence was, that I lost my appetite.[33] *Hence we see the pernicious effects of chewing and smoking tobacco.* I am of opinion, that *smoking tobacco is very pernicious to lean and hypochondriacal persons,* by destroying their appetite and weakening digestion. When this celebrated plant was first brought into use in Europe, it was cried up for a certain antidote to hunger; *but it was soon observed, that the number of hypochondriacal and* CONSUMPTIVE PEOPLE *were greatly increased by its use.*"[34] The celebrated CULLEN says, a constant chewing of tobacco destroys the appetite by depriving the constitution of too much saliva.[35]

One of the KINGS of Spain was afflicted with a very offensive breath; to remedy which the physicians advised his majesty to chew a composition of gum mastic, ambergrease, and other perfumes; the use of which occasioned a great expenditure of saliva. The courtiers, either out of compliment to their sovereign, or, what is more probable, from the vanity of imitating their superiors, went very generally into the same custom. The consequence was, that they, who followed the fashion with most ardour, lost their appetites, and became emaciated, and *consumptions* increased so fast among them, that the practice was forbidden by royal edict.

Some do not eject the saliva; but prefer swallowing the nasty mixture, which seldom fails to induce faintness, palpitations of the heart, trembling of the limbs, and sooner or later some serious chronical inconvenience.

After what has been said, who can doubt of the bad effects of constant application of powdered tobacco to the delicate membrane of the nose; especially if they know, what a thin partition divides the olfactory cavity from the brain?[36]

I have been a Professor in this University twenty three years, and can say, as a physician, that I never observed so many palid faces, and so many marks of declining health; nor ever knew so many hectical habits and consumptive affections, as of late years; and I trace this alarming inroad on your young constitutions principally to the pernicious custom of *smoking* CIGARRS.[37]

It is allowed by all, that since the foundation of this college the custom of smoking never was so general; it is conceded by all, that individuals, never pushed the fashion to such excess; and it is confessed by all, that the inhabitants of this place never appeared so palid, lanquid, and unhealthy. I will not say with some, that symptoms of languor have been discernible in your public performances; nor am I disposed to attribute it wholly to the causes mentioned in this lecture. I believe some of you study more, than is consistent with health; and exercise less, than is necessary for persons of your age. I feel a particular solicitude for such worthy characters as become sickly by indiscreet diligence; and I entreat them to consider, that the habit of smoking increases *muscular* indolence. Nor is this all — Smoking creates an unnatural thirst, and leads to the use of spiritous liquors. I will not vouch for the truth of the common observation, that great smokers are generally tipplers. They appear to be however different strands of the same rope.

Do you not GENTLEMEN, see clearly, that this nasty, idle custom includes the insidious effects of indolence; the deleterirous effects of a powerful narcotic fumigation; and the pernicious effects, consequent to the use of ardent and vinous spirits, destructive agents to men, but which act with redoubled force on the more susceptible frames of youth. I appeal to experience,

I ask whether he, who indulges himself in this way, does not awake in the morning hot, restless, and dissatisfied with himself? The sound of the bell grates his nerves. Even the

"Prime cheerer, light,
"Of all material being first and best,"

is an unwelcome intruder. He dresses with languor and fretfulness; his mouth is clammy and bitter; his head aches, and his stomach is uneasy, till composed a little by some warm tea or coffee. After stretching and yawning, he tries to numb his irksome feelings by a *cigarr* and a glass of wine, or a little diluted brandy. These disagreeable sensations will however come and go through the course of the day in spite of all his soporifics. By evening a handful of *cigarrs,* a few glasses of wine &c. remove by their stronger stimulus these troublesome sensations; when he tumbles into bed, and rises next morning with similar feelings, and pursues the same course to git rid of them. Does this look like a faithful extract from the diary of *"a Blood"*?

I am entirely convinced, that smoking and chewing injures ultimately the hearing, smell, taste, and teeth. *"Good teeth,"* says Hippocrates, *"conduce to long life"; because* he, who does not masticate his food properly, and mix it thoroughly with a due portion of saliva, will find his digestion fail; and this failure will gradually open the avenues to death.

The practice of smoking is productive of indolence, and tends to confirm the lazy in their laziness. Instead of exercising in the open air, as formerly, you sit down before large fires and smoke tobacco. This hot fumigation opens the pores of the head, throat, neck, and chest; and you pass out in a reeking sweat into a damp, cold atmosphere; the patulent pores are suddenly closed; hence arise disorders of the head, throat and lungs. These causes, cooperating with those, already mentioned, produce those hectical symptoms and consumptive complaints, that have been multiplying among you to an alarming degree; for this nasty custom includes the destructive effects of indolence, and the pernicious effects of the too frequent use of vinous and ardent spirits; agents, destructive to full grown men; but which act with redoubled force on the more susceptible frames of young gentlemen in the spring of life.

Some have said, and the observation carries with it a handsome compliment, "that smoking cannot be an evil custom seeing most of the clergy follow it." I am mortified that such authority can be adduced to oppose our advice. I will nevertheless venture to warn you, who expect to be cloathed with the sacred function against this inconvenient practice, until you are at least fifty years of age. As a sedentary man advances in life, he perspires less, while his lungs labour more. There is an accumulation of viscid phlegm among the inert and almost insensible solids of the lungs in elderly people, which in our cold months, especially in February and March, produces a kind of *chronic catarrh* or humoral asthma; for which smoking is beneficial. Here tobacco is a safe and efficacious pectoral. There is however a doleful difference between the case of a man of sixty five taking three or four pipes of tobacco in twenty four hours, and a boy of seventeen, who uses ten or a dozen cigarrs in that time. In one the cold and inert fibre is warmed and animated to throw off an offensive load; in the other it is adding fuel to fire; and irritating glands already sufficiently stimulated by his youthful nature.

[38] The gentlemen of the clergy drink sparingly even of wine, but many, who indulge in smoking, drink enormous quantities of hot tea,[39] which BOERHAAVE observes to be one of the pernicious consequences of smoking tobacco; as it assists to bring on hypochondriac and other dismal disorders. By forbearing to do what may innocently be done, we may add hourly new vigour to resolution. I can hardly believe there ever was a rigidly virtuous man, who became a slave to tobacco. To set the mind above the appetite, says the British moralist,[40] is the end of abstinence; and abstinence is the groundwork of virtue. For want of denying early and inflexibly, we may be inticed into the recesses of indulgence, and sloth and despondency may close the passage to our return.

[41] I hope that those of the clergy, who follow remarkably this custom, will receive kindly, what I utter seriously, respectfully, and affectionately. Strengthen, I beseech you, the hands of these youth, to relinquish a habit, which you know requires some exertion. If you want an excitement, look at that consumptive young man, whose emaciated figure strikes you with horror; see his forehead covered with drops of sweat; his cheeks painted with a livid crimson; and his eyes sunk; his pulse quick and tremulous; his nails bending over the ends of his fingers; and the palms of his hands dry and hot to the touch. His breath offensive, quick, and laborious; his cough incessant, scarcely allowing him time to tell you, that he smoked cigarrs without number, drank brandy and water, and wine; played daily on the flute[42]; and coming one night from a crowded musical meeting, caught cold; which being neglected,

brought on a cough, short breath, expectoration of purulent matter, and night sweats; which soon hurried him on to what you see.[43]

Of the *seemliness* or *decency* of the practice of smoking and chewing tobacco more may be said, than you will have patience to hear. BOERHAAVE observes, that "it is allowed by the universal consent of the more civilized nations, that spitting in company is both unmannerly and nasty; insomuch that among the inhabitants of the East it was held in the highest detestation and abhorrence!" A physician should never use tobacco in *any form*, as some weak patients will faint at the smell.[44]

The fashion of smoking tobacco was introduced into England by *Sir Walter Raleigh* in the reign of JAMES I. The custom was followed by almost all the nobility and high officers of the realm to the great dissatisfaction of the fastidious monarch. So universally prevalent was this fashion, that his majesty could not readily find any one to write or preach against it. He therefore wrote a tract himself, which he entitled *"a counter blast to Tobacco,"* a copy of which may be seen in the library of this University. After exposing in strong language the unhealthiness and offensiveness of this practice, he closes with this ROYAL COUNTER BLAST. — *"It is a custom, loathsome to the* EYE, *hateful to the* NOSE, *harmful to the* BRAIN, *dangerous to the* LUNGS; *and in the black, stinking fume thereof, nearest resembling the horrible stygian smoke of the pit, that is bottomless!"*

To conclude. — The moral, to be deduced from our whole Lecture is, *the necessity of avoiding all* predisposing *causes to* NERVOUS DISORDERS; *and obviating the* remote *causes of* CONSUMPTION. Quit then this pernicious habit, I entreat you. — Take all your cigarrs and tobacco, and in some calm evening carry them on to the common, and there sacrifice them to *health, cleanliness,* and *decorum.* — But, should perversity withstand all the arguments adduced, we have yet one in reserve, that is irresistible. The dangerous tendency of these practices no one can doubt; therefore abandon the custom, LEST YOU PIERCE WITH ANGUISH THE HEARTS OF YOUR AFFECTIONATE PARENTS!

FINIS.

Footnotes

[1] A *public* lecture means here an address to all the students of the University of every rank and class.

[2] Water was thought by *Hippocrates* to be an article so important to the health of a people, that of his treatises, one of the most elaborate is "on *air* and *water*"; which includes soil and situation. Had the builders of *Jericho* known and followed the rules of Hippocrates, they would not have complained to the prophet ELISHA, that although "the situation of the city was pleasant, the water was naught and the ground barren."

[3] This worthy gentleman was professor of Divinity. His death, which happened in June 1794, the author has never ceased to lament. To him we principally owe the MEDICAL INSTITUTION, founded here in 1782. By opening a correspondence with *Principal Robertson* and the *Medical Professors* at Edinburgh, he matured the plan, and lived to see it flourish. Dr. WIGGLESWORTH first suggested to the CORPORATION the idea of establishing *Lectures* on *Natural History.* Confidence in his *prediction* enabled the Lecturer to continue them from that period (1788) to the present.

[4] PROFESSOR PEARSON remarks in a lecture, published since this was delivered, that "from 1769 to 1796, a period of twenty seven years, but nine deaths took place among the undergraduates. But from 1796 to the present time, a period of little more than eight years, sixteen students terminated their probation for eternity, before they had completed their academic course; and, what deserves particular notice, most of them died of *consumption.* During the period, first mentioned, the deaths were to the years, as 9 to 27, or as 1 to 3, that is, one death in three years. During the last period, the deaths have been to the years, nearly as 16 to 8, that is two deaths in one year. Hence it appears, that the number of deaths among undergraduates during the last eight years, compared with that of the preceding twenty seven years, has increased nearly in a sixfold ratio. A result, worthy of serious consideration; expecially, when it is added, that four of these melancholy events took place in one year, and six of them in one class. In this connexion I am constrained to add that, during the two last years, and soon after receiving the first honors of this University, four others have been numbered with their deceased companions, alike victims to consumption."

[5] That species of jaundice, especially termed Icterus *mucosum.* See Van Swieten §950.

[6] That species, denominated asthma *flatulentum;* which, like the gout, palsy, and apoplexy, takes its origin from long continued affections of the stomach.

[7] See an Essay of Dr. Cogan's on the subject of health.

[8] While man, quadrupeds, and birds, select and inspire *oxygenous gas* from the atmosphere, by their *lungs,* fish inhale the same vital principle from the water by their *gills.*

[9] *Marshal Biron,* who had a remarkable keen appetite, was killed by a cannon ball an hour after dinner. On opening the body not the least trace of food was to be found in the stomach.

[10] DR. PRIESTLEY was the first who demonstrated the existence or identity of oxygenous gas, or, as he called it, *dephlogisticated air.* That there was such a principle in the atmospheric air was known long before. Not to mention Dr. Hook and Mayow, who were contemporary with Boyle, if we turn to the article AIR in Jame's Medical Dictionary, which article is compiled from the writings of *Arnaldus de Villa Nova,* and *Boerhaave,* we shall find the following account of the *acidifying* principle in the atmosphere. The upper surface of the blood says Boerhaave, that is exposed to the air is of a bright scarlet, while in every other part, which the air does not come at, grows as black, as the blood of the cuttlefish; and yet as soon as ever this black part is laid open

to the air, the black colour is immediately changed into a scarlet. This vivifying principle in air, so necessary to the support of flame and fire, as well, as animal and vegetable life, seems by every phenomenon to be the *universal acid*, distributed through the entire atmosphere, in a certain proportion; insomuch, that no portion of air seems to be within it. It is this acid, that corrodes the baser metals. By this acid the calx of vitriol, of aslum, and the earth, from which nitre has been procured, are again replenished in such a manner, as to be capable of producing acid spirits afresh. There is reason to suspect, that flowers are obliged to this acid of the air for their beautiful colours. Dyers of scarlet cannot strike that colour without the assistance of an acid. Hence the phenomenon of the surface of the blood, when exposed to air contracting a redness, may be in some measure accounted for. All concerned in dying observe, that a cloudy moist air interferes with the beauty and vividness of their colours; and that a serene sky exalts them, and makes them more elegant. This acid of the air finds some way of mixing with the blood. It is believed, that this *grand operation* is performed in the lungs, and that then the blood acquires a scarlet colour. *In what does this differ from the modern doctrine of* OXYGEN?

To persuade students of the present day to peruse any medical or chemical book, written anterior to 40 years, is not an easy task. They suffer under a notion, that all chemical and medical authors, prior to Black and Cullen, composed their works in the dark. Even the writings of the immortal Boerhaave are deemed but of little worth! It has been perhaps at the risk of reputation that I have recommended from time to time the writings of *Harvey, Ruysch,* and *Willis* in anatomy; *Aretaus Cappadox, Prosper Alpinus,* and *Sydenham* in the practice of medicine; and *Wiseman* in surgery; *Arnaldus, Van Helmont, Stahl,* and *Boerhaave* in chemistry; *Aldrovandus* and *Gesner* in natural history; *Malpighius* and *Grew* in botany; *Hook, Hales,* and *Boyle* in natural philosophy; and *Lord Bacon* for the whole Encyclopedia.

He, who studies for example the old chemists, will thereby preserve his mind from being overwhelmed with admiration for the labours of *Black, Lavoisier* and *Priestley,* great and important as they are. Medical students and young physicians thirst after NEW publications, without considering that bookmaking is now become a trade in Britain; where, instead of increasing the *stock* of knowledge, they are only pouring it out of one phial into anouther for sale.

[11] *Arnaldus de Villa Nova,* an excellent physician, chemist, and philosopher, who flourished about the year 1300, was not ignorant of this exhilirating *something* in the atmosphere. He speaks of a clear, pure air, that makes the heart glad, the mind serene, the body lightsome, at the same time, that it accelerates digestion. He speaks of a contrary condition of the air, which disturbs the heart, darkens the mind, makes the body heavy, and retards and hinders digestion.

[12] It can be distended so as to contain five quarts, and contracted so as to contain less than half a gill.

[13] See CULLEN's distinction between *Dyspepsia* and *Hypochondriasis* MCLXXII to MCLXXV.

[14] Ut curvi norma rectum, ita morbi sanitas, says Gaubius — that is, as a curve line is the reverse of a strait, so is health of a disease.

[15] If the reader will cast his eye over *Dr. Cadogan's* treatise on the *gout,* he will see how closely we have adhered to his principles, in this part of our lecture.

[16] See Cadogan on the gout.

[17] From δύς, bad or difficult, and πέπτω, to concoct.

[18] See Cullen's chap, on Dyspepsia.

[19] Spectator No. CXV.

[20] Cadogan.

[21] Cadogan was a disciple of the *humoral* pathology. To feel the full force of his reasoning, the medical student must advert to the distinction between plethora *ad volumen,* and plethora *ad vires.* See Gaubius. Path. Institut.

[22] Opportunities of looking into the stomach of a living subject are very rare indeed. I remember but two instances on the records of medicine. One was a woman, who was in the general hospital at Vienna in 1798. She had her stomach perforated by a wound, which could not be closed up. Through this wound her food might be seen. When any indigestible food created uneasiness, as *sour crout,* she took the oppressive food out with her fingers, and washed out her stomach with water, and this always relieved her, and revived her appetite. Milk was observed to crudle instantly, except when she had carefully rinced out her stomach. In this case says *Dr. Helme,* the coagulation did not take place, till after some time, for want he supposes of gastric liquor. The coagulation could be expedited by irritating the inner surface of the stomach with the finger. Asses milk was longer in coagulating than cows milk. The last coagulated in a few moments. Eggs, and cheese were quickly digested, but not so soon as flesh meat. Vegetables in general were longer undergoing this process; of these potatoes, and carrots passed off soonest.

[23] Elixir of vitriol, if long continued, has a pernicious effect on the stomach.

[21] See page 363.

[25] See page 364.

[26] Beside the ordinary consumption, which is *a coughing up of purulent matter from the lungs with a hectic fever,* there is a *nervous* consumption, a marasmus, or *Tabes dorsalis,* of which these are the most striking symptoms; — an irksome feeling of the whole body, with an increased sensibility and moroseness of temper. A painful tenderness of the eyes, with a dimness of sight; and sometimes a suffusion of tears; a ringing of the ears; a disagreeable feeling in the skull, as if the membranes of the brain were twisted. Not only a disinclination to study, but an inability to concentrate his ideas on any subject. With a failure of digestion, there is a sinking at the pit of the stomach, and a sensation, as if the whole tract of the bowels, with the *vesica urinaria,* were pulled down, and even scraped. There is a dull pain in the back of the neck, a frigid, disagreeable, shuddering sensation passing down the back, alternating with internal heat. These symptoms are more distressing in the morning. The causes continuing, the function of digestion is ruined; a leanness and dryness of the body ensue; the countenance has a peculiar sallow cast, with a physiognomy expressive of unhappiness. *Frons lata parum et deject lumina valtu.* Virg. — For more information read TISSOT.

[27] Until within a few years, it was so constant a custom for the collegian to bottle off his barrel of cider, that cellar rent was a charge in each quarter bill; but no such thing exists at present. The cellars are unoccupied, while the "*studies*" contain the QUART-o's.

[28] Of ARDENT SPIRITS and WINE —

The art of procuring ardent spirits by distillation was a discovery of the Arabian chemists. They first obtained it from *rice;* whence it took its name *arrac.* At present it is generally procured by the distillation of fermented liquors. In France it is drawn from wines. In England and in Germany from malt liquors; and in this country and the West India Islands from sugar and from mollases. This ardent spirit, from whatever subject it is obtained, is found, if freed from the phlegm and gross oil, to be essentially the same. By repeated distillations this spirit is purified, when it obtains the Arabic name of *alcohol.*

Wine is the fermented juice of the grape, and contains *three* different matters; First a portion of MUST or unassimilated matter. Second a portion of *Proper* WINE, in which by means of fermentation a quality of alcohol is produced. Third a portion of VINEGAR, produced by too active or too long protracted fermentation. In new wine the *must* will be most abundant; as fermentation advances the portion of genuine *wine* will be more considerable; if fermentation has all along been properly managed, *vinegar* will not appear in any considerable quantity. From the proportion of these several matters, depending on the period and state of the fermentation, the *qualities* of wine may be ascertained. See NEUMANN's Chem. Lewis' Mater. Med. and Motherby's Dict.

The ŒNUS or wine of the antients; that, which PAUL recommended, as good for the stomach, was a very different liquor from the wine, drank by the English, Irish, and Americans. The wine of the antients was the pure juice of the grape, rendered active by fermentation; for they were totally ignorant of ardent spirits; whereas our strongest wines contain a fourth part of this fiery spirit, while many of the cheap ones are a vile mixture of

deleterious articles, justly ranked among the remote causes of our *nervous* disorders, palsies, and apoplexies. If one gallon of our strongest bodied wines be submitted to distillation, it yields one quart of spirit, that will burn when thrown on the fire. The quantity of sharp vinegar, contained in the same portion of wine, is not so easily ascertained.

We will now present you with a few experiments, demonstrating the pernicious effects of spirituous and vinous liquors, first on the stomach of brutes and next on the human.

In *Bavaria* during the years 1797, 1798, and 1799, the scarcity of fodder compelled them to destroy a great number of horses, employed both for the purposes of war and of agriculture. Dr. Pilger availed himself of this opportunity, and made a number of cruel experiments on nearly two hundred horses with arsenic, corrosive sublimate, barytes, opium, belladonna, hemlock, laurel water, *distilled spirits, wine,* and *vinegar.* After giving horses brandy so as not only to exhilarate them but to make them stagger, and even to drop down; he found on opening them, that it shrivelled and contracted the stomach, gave a bloodshot appearance to the intestines, and produced congestions in the brain. But the effects of *vinegar* was the most remarkable. Concentrated vinegar excited the most dreadful spasms, and produced fatal symptoms. They became extremely weak before death; and in those, which were killed in this extreme weakness, the alimentary canal exhibited very little or no irritability on pricking its fibres.

That vinegar is destructive to the human stomach is known by its effects on plump, healthy females, who from a *silly* desire of looking delicate, that is *sickly,* swallow daily large draughts of vinegar. This *innocent* practice *only* ruins the digestive faculty, and thereby deprives the system of its requisite nourishment! The only standard of beauty is high health. Dr. Beddoes tells us that in some of the boarding schools in England, a keen appetite and its consequence *embonpoint* is held up by the mistress, as a dreadful evil; and that starvation and vinegar are encouraged, instead of being severely denounced. Emaciation, thus induced, leads to consumption.

From what has been said it appears, that some wine makes a twofold attack on our health and happiness. It attacks the stomach as wine, and returns to the charge in the form of vinegar. Hence in weakly stomachs, when the *ingesta* are composed chiefly of vegetables, and nearly on the point of acidity, a single glass of wine, nay half a glass, will turn the whole mass into so much thick vinegar. Then come *magnesia* and *lime-water* to neutralize the vinegar bottle! Who then but must see the absurdity of throwing a glass of wine into a *dyspeptic* stomach directly after a dinner, composed chiefly of vegetables? Yet it is constantly done to the unspeakable distress of the sufferer, agonizing with wind and acid. Physicians should endeavour to convince such patients that wind and acid are not the causes, but the consequences of a torpid, imbecil stomach. They should be told, that when a healthy stomach is moderately filled with vegetable and *well* roasted, or *well* boiled meat, neither *air,* nor *acid* is to be found in the whole alimentary canal.

OF THE PERNICIOUS EFFECTS OF WINE ON CHILDREN.

The best informed European physicians condemn the practice of giving wine daily to children. It has become a prevalent custom of late in America, to give a glass of wine to such children, as are old enough to sit at table with their parents. If the opinion of experienced physicians have no weight with parents the following well conceived experiment, being proof positive of the pernicious effects of wine, may possibly induce some to reflect a little on the subject.

A physician of great eminence in London gave to one of his children a full glass of sherry every day after dinner for a week. The child was about five years old, and had never been accustomed to wine. To another child, nearly of the same age and under similar circumstances, he gave a large China orange for the same space of time. At the end of a week he found a very material difference in the pulse, the heat of the body, the urine, and the stools of the two children. In the first the pulse was quickened, the heat increased, the urine high coloured, and the stools *destitute of their usual quantity of bile;* while the second has every appearance, that indicated high health. He then reversed the experiment; to the first mentioned child he gave the orange, and to the other the wine. The effects followed as before; — *a striking and demonstrative proof of the pernicious effects of wine on the constitution of children in full health.*

This accurately executed experiment is related by Mr. Sanford, Surgeon at Worcester in England, and quoted by Dr. Beddoes in his *Hygëia;* who thus remarks on it, "that the *deficiency of bile* is full evidence of the injurious effect of wine upon the digestive organs in this double experiment." Yet we find that some physicians have learned their patients to attribute these very complaints to a *redundancy of bile!* and therefore prescribe *salt of wormwood* and *rhubarb;* or *soap, rhubarb,* and *aloes,* inducing thereby a farther weakness of the digestive organs, the proximate cause of the disorder. My venerable preceptor, DR. FOTHERGILL cured such complaints with fresh made *porter.* By the time London porter arrives in this country it contains too much vinegar to be serviceable in these cases.

Mahomet with a view to temperance forbad his followers to drink wine; and in order to correct their savage custom of eating raw flesh, as do the Abyssinians at this day, he allowed them to eat any thing, that had *passed through fire;* meaning whatever had undergone the process of cookery. A century or two after his death, the chemists of his country discovered the art of drawing ardent spirits from *rice* by distillation. When these mahometans were reproached for intoxicating themselves with this spirit, which they called *arrac,* they replied, that *it had passed through fire,* and was therefore agreeable to the laws of Mahomet, as expressed in the Koran.

[29] GALEN was the first Greek writers, who mentions opium. It was but little used among the antients. *Paracelsus* and *Silvius de la Boie* brought it into vogue in Europe. *Sydenbam* used it first in small pox.

[30] NICOTIANA, so called from *Jacobus Nicotius,* ambassador to the court of Portugal from Francis II, king of France. *Nicotius* bought some seeds of this plant from a Dutchman in 1560, who had just brought them from America. From this seed the plant was produced in France. *Sir Francis Drake* carried it to England; and *Sir Walter Raleigh* first brought it into fashion. The dried plant was afterwards imported in great plenty from Tobago, and hence it obtained the name of *Tobacco.*

Linnaus places this genus of vegetables in the first section of his fifth class, which contains those plants, whose flowers have five stamina and one style, which expressed in botanical language is *Pentandria, Monogynia.* This genus has eleven species; one of which is called *Hyoscyamus* from its agreeing in several of its characters with the deleterious henbane.

Nicholas Monardus a German has written a folio on the virtues of tobacco. It is doubtless a valuable medicine, especially in cases where the *Digitalis* has been used without success. An English physician, Dr. Fowler, used a tincture of tobacco in 52 cases of dropsy, and found it efficacious in 49 of them. The same physician found it very beneficial in *Dysuries* from gravel. I have used it in such cases with satisfaction.

[31] See Mr. Mudge's essay on the *Vis Vita.*

[32] Boerhaave's Academ. Lectures.

[33] Females who spin flax, and the manufacturers of straw-bonnets suffer from the same cause.

[34] Boerhaave Academ. Lectures.

[35] Cullen's Materia Medica.

[36] Too constant use of strong *snuff* brought on a disorder of the head, which was thought to have shortened the life of a celebrated divine and accomplished gentleman; "CUJUS ETIAM A LINGUA MELLE DULCIOR FLUEBAT ORATION."

[37] *Cigarr,* from the Spanish *Cigarro,* a little roll or tube of tobacco; *Tabasi folia in tubulum convoluta.* A cigarr is a leaf of tobacco formed into a small twisted roll, somewhat larger than a pipe stem, of about 6 inches long. The smoke is conveyed through the winding folds, which prevent it from expanding; there is however a small aperture made through the middle by a wire. The cigarr preceded the invention of the pipe. The best come

from the Havanna; those most esteemed are made in the convents.

[38] THOMPSON.

[39] These paragraphs have been added since the delivery of the lecture.

[40] COFFEE and TEA are articles friendly to morals, seeing they frequently exclude the use of spirituous liquors. The French and Spaniards take coffee directly after dinner instead of wine; a custom, worthy of imitation. A physician is often asked, which is most wholesome tea or coffee? Either of them, made very strong, must be injurious; both, certainly suspend the inclination to sleep, and impede digestion. Tea or coffee of moderate strength, and drank with discretion, is found by experience friendly to the human constitution. *Old smokers* will sometimes drink a dozen dishes of tea, and destroy thereby the tone of their stomachs. *Young* smokers also suffer from the same cause. One of the most speedy methods of weakening the stomach is to smoke cigarrs, and at the same time *swill* tea or coffee, and eat an enormous pile of toast, swimming in butter. We have said already, that the use of the saliva was to assist with the bile to mix butter and fat with the watery part of our food; but in such a meal the saliva is either spit out or vitiated; and the incongruous mass is left to sour, because the principle mean of assimilation is withdrawn.

[41] Johnson.

[42] Playing on wind instruments as well as singing are pernicious to persons predisposed to consumption.

[43] Compare this with FOTHERGILL's description of consumption in LETTSOM's edition of his works.

[44] The custom of smoking has for a considerable time past been totally banished from all polite companies in England It is there confined to taverns and alehouses.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY....ANYWHERE

PLUS insurance for....
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

RHODE ISLAND AIR NATIONAL GUARD

PART TIME

MEDICAL OFFICER POSITIONS AVAILABLE

OPEN TO:
MEDICAL AND/OR
OSTEOPATHIC DOCTORS

CONTINUING MEDICAL EDUCATION

FOR MORE INFORMATION CONTACT:
COL (DR) BLAS MORENO
(401) 726-2555

"BEST PART-TIME JOB IN AMERICA"

PERIPATETICS

Paul Calabresi, chairman of the Department of Medicine and chief of medicine at Roger Williams General Hospital, has been elected to the Board of Trustees of New York Medical College.

• • •

The Miriam Hospital has appointed **Charles C.J. Carpenter** physician-in-chief. He has also been named professor of medicine at Brown. Previously, **Carpenter** was professor and chairman of the Department of Medicine at Case Western Reserve University School of Medicine and director of the Department of Medicine at University Hospitals of Cleveland. **Carpenter** is a prominent international figure in the study of the pathophysiology of enteric infections.

• • •

Hospice Care of Rhode Island has named **Henry A. McDuff, Jr.,** a Providence gynecologist and obstetrician, as its Medical Director. **McDuff** is presently a clinical professor emeritus at Brown University, an instructor at Women and Infants Hospital, and a member of the Board of Directors of the American Cancer Society, Rhode Island Division.

• • •

A partnership has been established between **Mel H. Epstein,** chief of neurosurgery at Rhode Island Hospital, and Richard Easton, chief of neurology at Rhode Island Hospital, to co-chair the newly formed Clinical Neuroscience Department at Brown. **Epstein** will chair the clinical department at Brown during the 1987 calendar year.

• • •

The Medical Scientific Advisory Council of the National Hemophilia Foundation has elected **Peter S. Smith** of Rhode Island Hospital as representative for Region 1. As medical director of the Rhode Island Hemophilia Center, **Smith** will assist in addressing critical medical and scientific issues for persons with hemophilia.

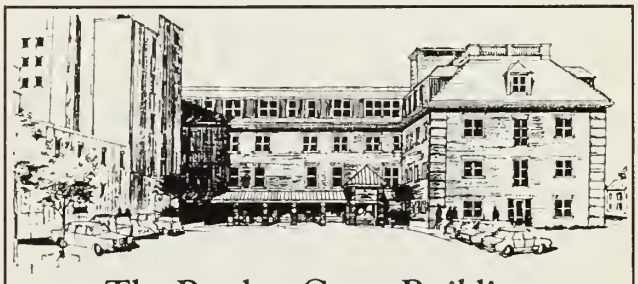
• • •

William Oh, pediatrician-in-chief at Women and Infants Hospital has been appointed acting chairman of the Brown University Department of Pediatrics until September 30, 1987. **Oh** has assumed departmental responsibilities while Leo Stern, department chairman, is on sabbatical leave.

• • •

The RI March of Dimes' Health Professional Advisory Committee has selected **Betty R. Vohr,** neonatologist and director of Women and Infants Hospital's neonatal follow-up program, as its chairman.

• • •



The Borden-Carey Building
Medical and Office Condominiums

NOW AVAILABLE FOR SALE
OR LEASE

Conveniently located at 19 Friendship St.,
Adjoining Newport Hospital

Individual Suites are now available for
interior design and tenant finish.

Priced to sell from $80,000 and to
lease for $15.00/s.f.

For further information call:

RE
Ryan Elliott

Ryan Elliott & Co. of Rhode Island, Inc.
401-331-0350

You got the wrinkles ironed out of that investment property financing in no time. How'd you do it?

My Private Banker. Perrier?

Do you have substantial assets, or an income that's on the way up? A Hospital Trust Private Banker can provide maximum response to your investment and real estate financing needs. Your Private Banker has significant expertise for significant goals.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Perrier is a registered trademark of Great Waters of France, Inc.

Equal Opportunity Lender

HAVE YOU HEARD? . . .

In the June *Archives of Neurology,* a two-year multicenter study concludes that natural human fibroblast interferon (interferon beta), administered intrathecally (injected into the spinal canal), is effective at easing multiple sclerosis (MS) flare-ups. The mean reduction in exacerbation rates for 34 MS patients receiving interferon beta was significantly greater than that for 36 control patients receiving a placebo. This was found by Lawrence Jacobs, MD, of the State University of New York School of Medicine, Buffalo, and colleagues in a randomized, double-blind study. The study says, "interferon beta therapy was well-tolerated, and the side effects were clearly acceptable for the benefits achieved" in 95 per cent of the recipients. The results confirm those of an earlier preliminary study, say the researchers, but they cannot explain the mechanism by which the interferon seems to work.

• • •

Spasmodic dysphonia, in which a patient's vocal folds pinch together when trying to speak, giving the voice a strained strangled quality, may be temporarily relieved through injection of a form of the toxin that causes botulism. This from a preliminary study in June's *Archives of Otolaryngology-Head and Neck Surgery.* None of the several therapies used in this disabling condition — associated with neurologic problems — is curative, though, and results vary. Robert H. Miller, MD, now of the Tulane University School of Medicine, New Orleans, and colleagues used a special hypodermic needle to inject botulinum A toxin into the vocal folds of two patients incapacitated by spasmodic dysphonia. Both experienced significant improvement without complication. The selective muscle weakness caused by the treatment is not permanent, the study says, but "the injection can be repeated as needed on an outpatient basis."

• • •

It is suggested through a study reported in June's *American Journal of Diseases of Children, AJDC* that children cured of Hodgkin's disease, a lymph system cancer not uncommon in young people, lead well-adjusted lives as young adults. Forty Hodgkin's patients who had finished their therapy five years earlier and were in complete remission were interviewed by Abby L. Wasserman, MD, of St Jude Children's Research Hospital, Memphis, and colleagues. The educational achievement of those interviewed was statistically better than that of comparable populations, and they exhibited no increased evidence of depression or other psychiatric disorders. The study went on to say that "almost all subjects believed they had benefitted in some way from their experience with cancer." However, there were problems cited — treatment side effects were the "worst thing" about the disease, and 40 per cent of the survivors reported unpleasant experiences in school. Discrimination in employment or in obtaining life or health insurance were some of the current concerns.

• • •

The Joint Commission on Accreditation of Hospitals will require healthcare organizations to have policies in place concerning withholding resuscitative services to patients, beginning January 1, 1988. The proposed standards were approved at the April 25 meeting of the Joint Commission's Board of Commissioners. The new standards on "Do Not Resuscitate" decisions will be included in the Joint Commission's *Accreditation Manual for Hospitals and Consolidated Standards Manual.* Dennis S. O'Leary, MD, Joint Commission president, states that the need for healthcare organizations to address complex medical, ethical, and legal ramifications of withholding resuscitation are reflected in the new standards. Facilities need to examine the decision-making process and the

roles of physicians, nurses, and other professionals, according to O'Leary.

• • •

Hewlett-Packard Company has introduced a new ECT monitor (HP 78351T) which will provide high-quality patient-monitoring capabilities for the emergency room, intensive-care unit, operating room, specialty clinic and other areas where reliable ECG monitoring is important. Because of new manufacturing efficiencies, HP can provide the capabilities and reliability of the new monitor at a low price. It is also easy to use, with automatic setup and flexible configuration. Many features are offered with the HP 78351T including intelligent cardiotach, electrosurgery-interference suppression, super-raster display, softkey operation and self-diagnostics. The monitor also has an optional recorder interface, Option J10.

• • •

Twenty new drugs and four new biotechnology products were approved by the FDA in 1986 for the US pharmaceutical industry. Products to treat heart disease, arthritis, anxiety, ulcers, infectious disease, psoriasis and hairy cell leukemia are among those approved. The four biotechnology-derived products include a monoclonal antibody to prevent rejection of kidney transplants, a genetically-engineered vaccine against hepatitis B, and two alpha interferons to treat hairy cell leukemia. The average time from the discovery of the chemical until approval of the 20 new drugs by the FDA was more than ten years. Of that ten years, FDA's review took 34 months.

• • •

Genetic Technology News®, the monthly update service for executives interested in applications of genetic engineering, has forecast that breeders could use genetically engineered cattle, swine, and chickens to add $700 million to the value of their sales to US farmers. Genetically engineered animals could require less feed. This would result in lower costs for producing meat, milk, or eggs. The quality of meat could also be improved as well as animals becoming more disease resistant. The major obstacle in reaching these improvements is not technological development, but possible government restrictions.

Opponents of animal genetic engineering are not concerned about safety. Instead, it is believed by one group to be unethical to use genetic engineering to move genes from one animal to another. Another group of opponents, small dairy farmers, fear that genetically engineered animals will be advantageous only to large dairy farmers, thus driving small farmers out of business.

Genetic Technology News® believes that any US regulatory restrictions will be resolved by 1995 and genetically engineered animals will have made a substantial impact on US livestock and poultry production. Through a ruling by the US Patent and Trademark Office, a genetically engineered animal can now be patented. This will make commercial development of genetically engineered animals much more attractive. Patent holders can protect their inventions from piracy through detection with DNA technology.

• • •

A UNIMED Pharmaceutical, **Marinol®** (dronabinol, a synthetic cannabinoid), was introduced for sale in the United States in July 1986 through Roxane Laboratories, Inc., a member of the worldwide Boehringer Ingelheim group of companies and a leader in the management of pain for cancer patients. Marinol's® role in treating nausea and vomiting induced by cancer chemotherapy is being expanded through additional studies. Initial clinical data demonstrate that Marinol® is synergistic with other antiemetics currently in use for cancer chemotherapy patients. Clinical data indicate potential for Marinol® in controlling appetite loss and weight loss, a serious problem affecting advanced cancer patients. An initial Phase II clinical study is underway at Fox Chase Cancer Center in Pennsylvania.

• • •

The re-formulation of **Opticrom®,** 4% Ophthalmic Solution (cromolyn sodium ophthalmic solution), has been announced by Fisions Corporation of Bedford, MA. The new formulation removes the preservative, 2-phenylethanol (2-PE), to enhance patient comfort. According to Dr Bernard Berman, Chief of Allergy at St Elizabeth Hospital in Boston and a faculty member of Tufts New England Medical Center, "Opticrom® is particularly useful in the treatment of red, itchy eyes that often accompany an allergic reaction." Dr Berman also noted cromolyn sodium is thought to be a safe medication for use by all physicians because it is free of side effects. Opticrom® is an antiallergic medication intended for topical application to the eyes. It is believed to act by stabilizing the membranes of ocular mast cells, thus preventing their degranulation and release of pharmacologic mediators in response to contact with antigens and other irritants.

• • •

The specific protein most hemophiliacs need to control bleeding episodes, the purest form of Factor VIII, will soon be available nationwide. Compared with 97 per cent for this new product, Factor VIII products currently on the market have a purity level of only 2 per cent. A newly invented proprietary purifaction process uses proteins, produced by sophisticated hybridoma techniques, that are designed and constructed to have unique specificity characteristics. In addition to the fact that patients lower their risk of exposure to viral transmissions, this product is devoid of extraneous proteins, normally found in today's coagulation factor concentrates, that are thought to have adverse long-term effects on the immune system of hemophiliac patients. The average dose can be as low as 2.5 ml, depending on the patient's size and weight, and is administered via an ordinary injection. This is particularly important for parents of hemophiliac children who must now administer dosages as high as 60 ml in a slow controlled infusion that is at least 10 minutes long.

MEDICAL SUITE AVAILABLE FOR RENT

1240 square feet
ample parking

Barrington Medical Center
East Providence

Call 433-2400

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

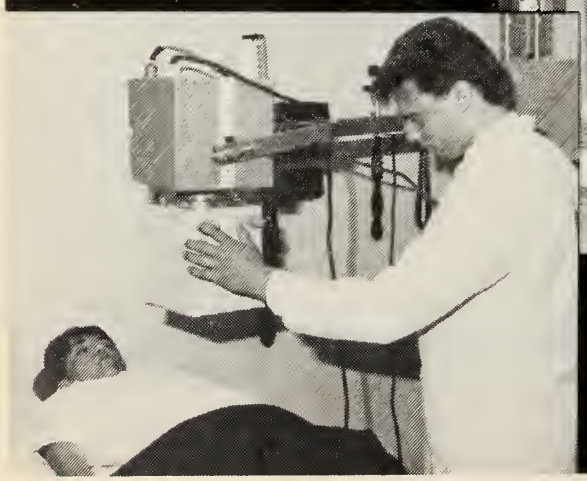
We've become the largest full service medical lab in Rhode Island...*because:*

- ✔ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✔ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✔ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✔ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

BOOKS RECEIVED

The ABCs of Prescription Drugs, by Edward Edelson, Doubleday and Company, Inc., New York, 1987, 275 pp., $12.95.

". . . provides . . . the most essential information . . . about today's most commonly prescribed drugs — arranged for quick reference according to the most common illnesses or conditions for which they are prescribed. Comprehensive and authoritative . . . in practical, layman's terms — general precautions, possible side effects, basic safety and storage information, comparison of generic and brand-name drugs, special advice . . . round out an invaluable handbook."

Clinical Electro-Cardiography: A Primary Care Approach, by Ken Grauer, MD and R. Whitney Curry Jr., MD, Medical Economics Company, Inc., Oradell, NJ, 1987, 544 pp., $24.95.

". . . a comprehensive guide for primary care physicians on ECG interpretations. . . . The problem-solving, clinically oriented approach leads to enjoyable reading and high retention. Includes a handy illustrated reference guide to much of the diagnostic data that can be detached for use as a pocket guide. Complete with self-testing review exercises, case studies, over 250 tracings and a clearly written test, this book is ideal for primary care physicians, medical students, residents and nurses."

Current Treatment of Ambulatory Asthma, edited by Guy A. Settipane, MD, the New England and Regional Allergy Proceedings, Providence, RI, 1986, 235 pp.

"Concerned with elucidating the specific and differing daily needs of each patient, the goal being prevention. Practical, concise, informative."

Malpractice Depositions: Avoiding the Traps, by Raymond M. Fish, PhD, MD and Melvin E. Ehrhardt, MD, JD, Medical Economics Company, Inc., Oradell, NJ, 1987, 152 pp., $24.95.

". . . provides essential information on how to handle the tricks and tactics one is likely to encounter when being sued, preparing physicians to deal with time-consuming, confusing, upsetting and potentially damaging deposition techniques. Written by two well-known leaders in the field who have planned and developed many successful malpractice defenses, this is the first authoritative source for deposition information."

Medical Journalism: The Writing, Design and Production of Local Medical, Pharmaceutical and Hospital Publications, edited by Craig D. Burrell, MD, Sandoz Corporation, New York, NY, 1986, 250 pp.

" . . for the physician who devotes a few hours a week as editor of a medical society magazine or newsletter, the executive director who produces a publication as part of a medical society total program, and the full-time medical journal staffer."

The Multiple Sclerosis Diet Book: A Low-fat Diet for the Treatment of M.S., by Roy Laver Swank, MD, PhD and Barbara Brewer Dugan, Doubleday and Company, Inc., Garden City, New York, 1987, 391 pp., $19.95.

"Swank and Dugan provide complete background information on the development of the . . . low-fat diet that works in reducing the number and severity of relapses in M.S. patients. There are also sections on . . . the lifestyle of the M.S. patient, tips for sticking to the diet, equipping the kitchen, shopping for healthful foods, eating out, and keeping careful dietary records."

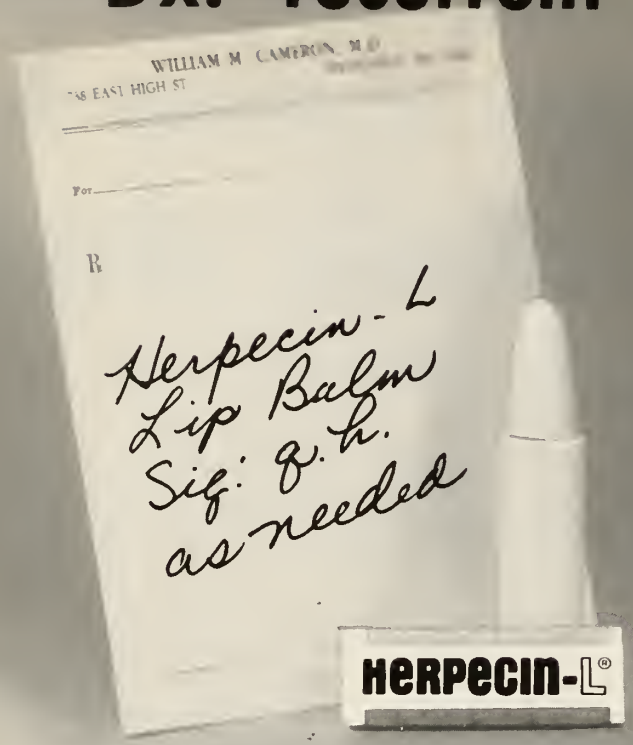
The New England Journal of Medicine, Massachusetts Medical Society, Waltham, MA, 1986, 109 pp.

A special edition of New England Journal of Medicine and Surgery and the Collateral Branches of Science, January 1812, Volume 1, Number 1, in celebration of their 175th anniversary.

Overcoming Breast Cancer, by Genell J. Subak-Sharpe, Doubleday and Company, Inc., Garden City, New York, 1987, 181 pp., $16.95.

"Up-to-date, concise, authoritative, complete information on risk factors, self-examination, diagnosis, staging — what it means for treatment and prognosis, surgical procedures, chemotherapy, hormone manipulation, the role of nutrition, breast reconstruction — the medical and psychological facts. The multi-faceted approach practiced by physicians at Evanston Hospital of Northwestern University's McGaw Medical Center."

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

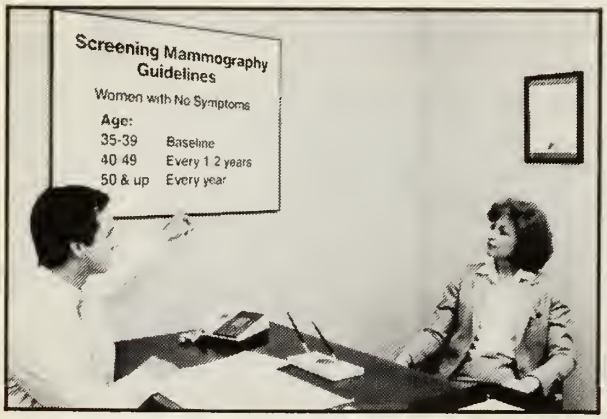
"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: **CAMPBELL LABORATORIES, INC.**, P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.



What will you tell her about screening mammography?

Many of your patients will hear about screening mammography through a program launched by the American Cancer Society and the American College of Radiology, and they may come to you with questions. What will you tell them?

We hope you'll encourage them to have a screening mammogram, because that, along with your regular breast examinations and their monthly self examinations, offers the best chance of early detection of breast cancer, a disease which will strike one woman in 10.

If you have questions about breast cancer detection for asymptomatic women, please contact us.

AMERICAN CANCER SOCIETY Professional Education Dept. National Headquarters 90 Park Avenue New York, New York 10016 or your local society

acr American College of Radiology 1891 Preston White Dr. Reston, Virginia 22091 (703) 648-8900

Are You Concerned About the Competence of a Certain Physician?

If so, the Peer Review Committee on Physician Competency can offer discreet and effective help. A standing committee of the Rhode Island Medical Society since 1985, the Peer Review Committee works in a completely confidential, supportive way to help assure that physicians consistently meet minimum acceptable standards of medical practice. The primary work of the Committee is to help physicians improve the quality of their care through education.

If you know a physician who can benefit from peer education in a particular area of medical practice, please write Dr. William Colaiace, Chairman, Peer Review Committee on Physician Competency, Rhode Island Medical Society, 106 Francis Street, Providence, RI 02906. For more information, call the Society at (401)331-3207. All referrals are held in strict confidence.

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

WARNING

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ L42

In Hypertension*... When You Need to Conserve K^+

Remember the Unique Red and White Capsule: Your Assurance of SK&F Quality

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).

Potassium-Sparing

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Over 20 Years of Confidence

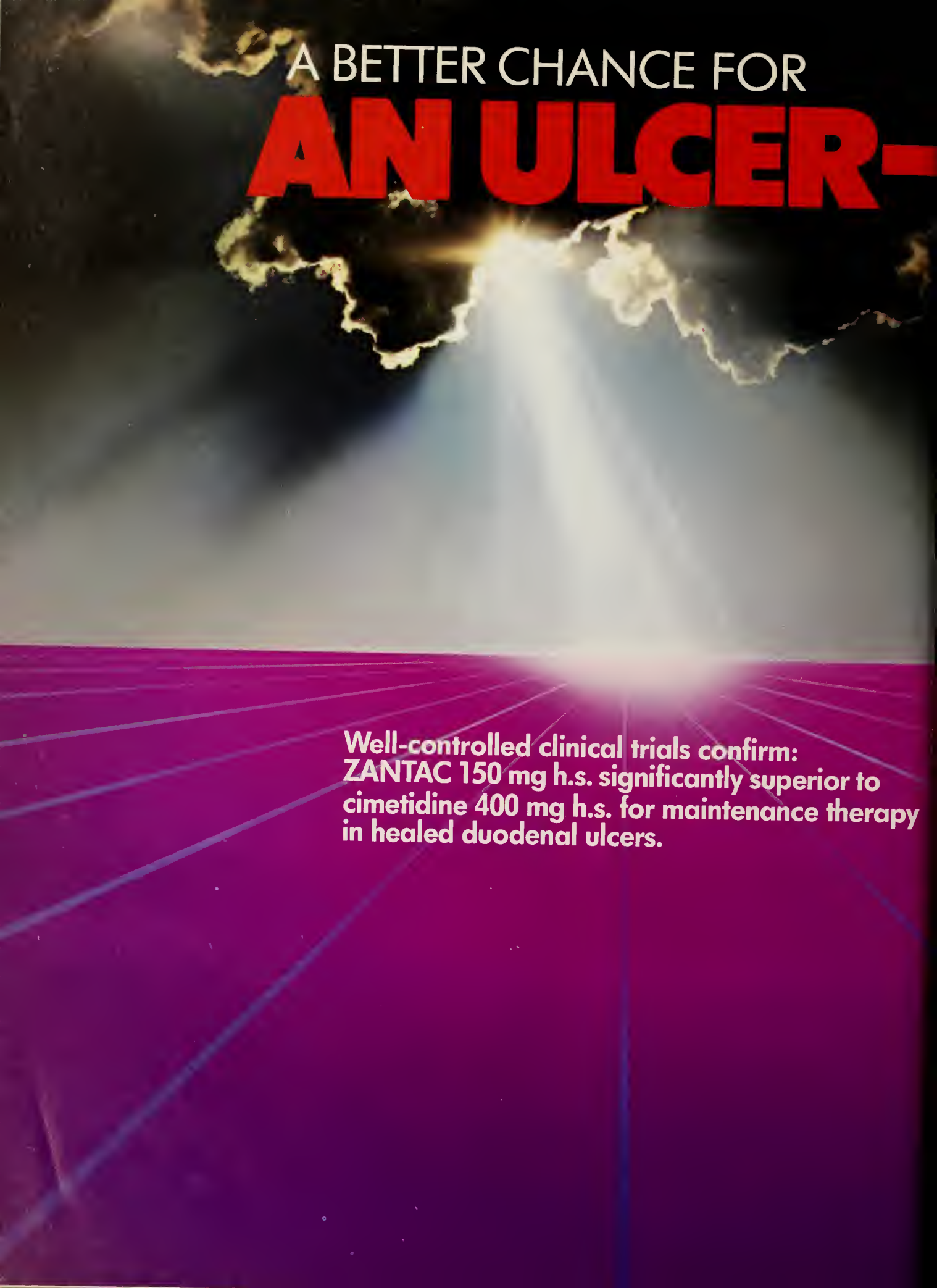
The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

a product of

SK&F CO.

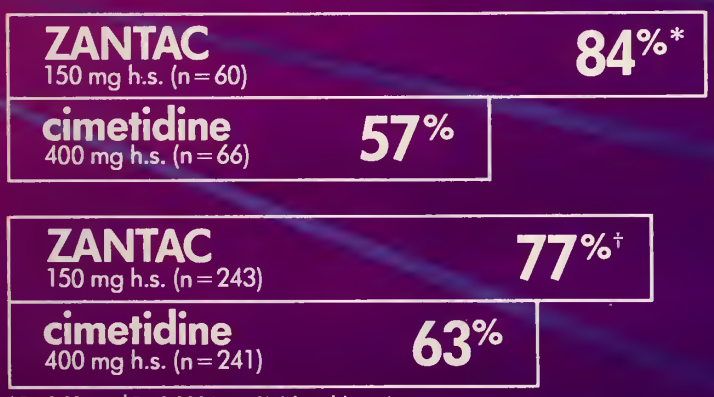
Carolina, P.R. 00630

© SK&F Co., 1983


A BETTER CHANCE FOR
AN ULCER-
Well-controlled clinical trials confirm:
ZANTAC 150 mg h.s. significantly superior to
cimetidine 400 mg h.s. for maintenance therapy
in healed duodenal ulcers.

FREE FUTURE

Percent of patients ulcer-free after 1 year of therapy



*P = 0.01 †P = 0.0004 % life-table estimates

All patients were permitted prn antacids for relief of pain.
Adapted from Silvis[1] and Gaugh[2]

These two trials[1,2] used the currently recommended dosing regimen of cimetidine (400 mg h.s.) and ranitidine (150 mg h.s.). A comparison of other dosing regimens has not been studied.
The studied dosing regimens are not equivalent with respect to the degree and duration of acid suppression or suppression of nocturnal acid.
The superiority of ranitidine over cimetidine in these trials indicates that the dosing regimen currently recommended for cimetidine is less likely to be as successful in maintenance therapy.

Zantac® 150 h.s.

ranitidine HCl/Glaxo 150 mg tablets

Glaxo / ROCHE®

See next page for references and Brief Summary of Product Information.

ZAN375 July 1987

References: 1. Silvis SE, Griffin J, Hardin R, et al: Final report on the United States multicenter trial comparing ranitidine to cimetidine as maintenance therapy following healing of duodenal ulcer. *J Clin Gastroenterol* 1985;7(6):482-487.
2. Gough KR, Karman MG, Bardhan KD, et al: Ranitidine and cimetidine in prevention of duodenal ulcer relapse: A double-blind, randomised, multicentre, comparative trial. *Lancet* 1984;ii:659-662.

ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY OF PRODUCT INFORMATION

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer.** Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD).** Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of therapy.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretary states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Although recommended doses of ZANTAC do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Lack of experience to date precludes recommending ZANTAC for use in children or pregnant patients. Since ZANTAC is secreted in human milk, caution should be exercised when administered to a nursing mother.

ADVERSE REACTIONS: Headache, sometimes severe, seems to be related to ZANTAC® administration. Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, premature ventricular beats, and arthralgias. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients.

In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanolicular or mixed, with or without jaundice.

There have been rare reports of reversible leukopenia, granulocytopenia, thrombocytopenia, and pancytopenia.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Incidents of rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison Syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

© Copyright 1983, Glaxo Inc. All rights reserved. October 1986

Glaxo

Glaxo Inc.
Research Triangle Park, NC 27709

What you get back is immeasurable.

Just five hours a week. Just 5% of your income. It's not much to give, to the causes you really care about. But that small investment could change somebody's life. And it's hard to imagine a better return than that.

INDEPENDENT SECTOR

Ad Council

In acute and chronic edema due to CHF

FOR PREDICTABLE CONTROL

- **Less potassium loss for a given amount of sodium excretion than with furosemide[1-3]**
- **Predictable dose response[4]**
- **Diuresis completed hours faster than with furosemide after oral dosing[5]**
- **Better GI absorption[6,7]**
- **Early evening dosing helps prevent nocturnal dyspnea**

As with all loop diuretics, excessive doses of BUMEX can lead to profound diuresis with water and electrolyte depletion, including hypokalemia, so serum electrolytes should be monitored.

Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets; 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

References: **1**. Flomenbaum W. *Am J Cardiol 57*(2):38A-43A, 1986. **2**. Broter DC, Fox WR. Chennovosin P. *J Clin Pharmacol 21* 599-603, 1981. **3**. Iber FL, Boum RA. *J Clin Pharmacol 21* 697-700, 1981. **4**. Henning R, Lundvoll O. *Eur J Clin Pharmacol 6* 224-227, 1973. **5**. Physicians' Desk Reference, 40th ed. Orodell, NJ, Medical Economics Company, 1986, pp. 939, 1480. **6**. Pentikainen PJ, *et al*. *Br J Clin Pharmacol 4* 39-44, 1977. **7**. *Lasix, A Review*. Somerville, NJ, Hoechst-Roussel Pharmaceuticals, Inc., 1980.

BUMEX®
(bumetanide/Roche)
0.5-mg, 1-mg and 2-mg scored tablets
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome.
Almost equal diuretic response occurs after oral and parenteral administration of Bumex. If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route.
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity.
CONTRAINDICATIONS: Anuria. Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion. Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment.
WARNINGS: Dose should be adjusted to patient's needs. Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients.
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risk to the patients.
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma. Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance. Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients.
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity. Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved. The potential for ototoxicity increases with intravenous therapy, especially at high doses.
Patients allergic to sulfonamides may show hypersensitivity to Bumex.
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary. Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets.
Hyperuricemia may occur. Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency. Bumex may increase urinary calcium excretion.
Possibility of effect on glucose metabolism exists. Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes.
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions.
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions.
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously.
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics.
Probenecid should not be administered concurrently with Bumex.
Concurrent therapy with indomethacin not recommended.
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage.
Interaction studies in humans have shown no effect on digoxin blood levels.
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity.
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
Bumetanide may be excreted in breast milk.
Pediatric Use: Safety and effectiveness below age 18 not established.
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease).
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting.
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection.
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium. Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy.
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts. Increases in urinary glucose and urinary protein have also been seen.
DOSAGE AND ADMINISTRATION:
Oral Administration: The usual total daily dosage is 0.5 to 2.0 mg and in most patients is given as a single dose.
Parenteral Administration: Administer to patients (IV or IM) with GI absorption problem or who cannot take oral. The usual initial dose is 0.5 to 1 mg given over 1 to 2 minutes. If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day.
HOW SUPPLIED: *Tablets*, 0.5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescription Paks of 30, Tel-E-Dose® cartons of 100. Imprint on tablets: 0.5 mg—ROCHE BUMEX 0.5, 1 mg—ROCHE BUMEX 1, 2 mg— ROCHE BUMEX 2.
Ampuls, 2 ml, 0.25 mg/ml, boxes of ten.
Vials, 2 ml, 4 ml and 10 ml, 0.25 mg/ml, boxes of ten.

P.I. 0985

Roche Laboratories
a division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

In acute and chronic edema due to CHF

A DIURETIC THAT GIVES YOU PREDICTABLE CONTROL

Bumex®
bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets; 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

Please see adjacent page for references and summary of product information.

Copyright © 1987 by Hoffmann-La Roche Inc. All rights reserved.

DISPLAY SHELVES

September 1987
Volume 70, Number 9

Rhode Island Medical Journal

SPECIAL EDITION to commemorate the 175th Anniversary of the Rhode Island Medical Society 1812-1987

CONTRIBUTIONS

397 A Discourse

401 Discourse on the Object and Utility of the Rhode Island Medical Society

409 The Annual Address

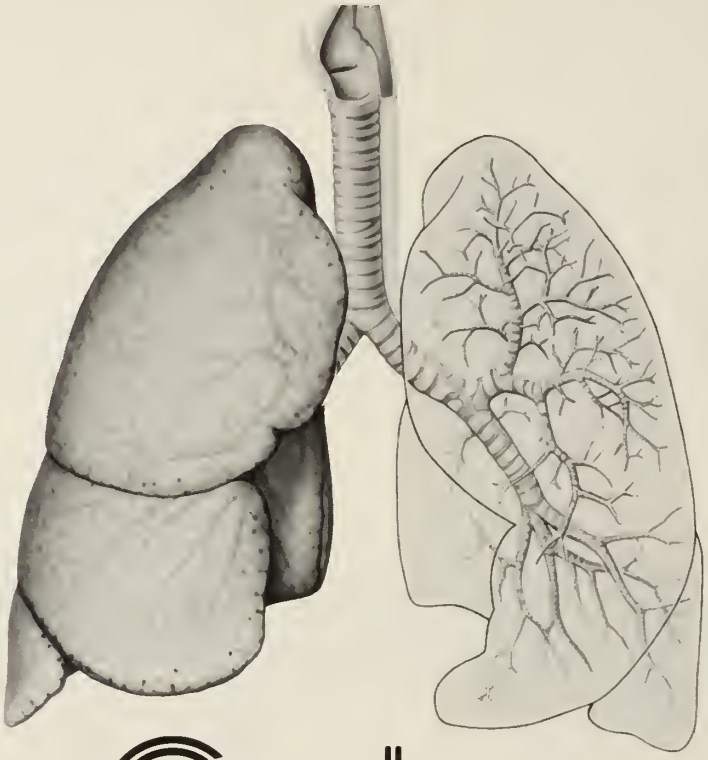
415 The Doctor's Image — Past, Present, and Future

395 EDITORIAL

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

OCT 1 1987

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, Streptococcus pneumoniae
(ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature tor prescribing Information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae,* and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Contraindication:
Known allergy to cephalosporins.

Warnings:
CECLOR SHOULO BE AOMINISTEREO CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS PENICILLINS ANO CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUOE ANAPHYLAXIS

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly).

[072886R]

PA 8794 AMP

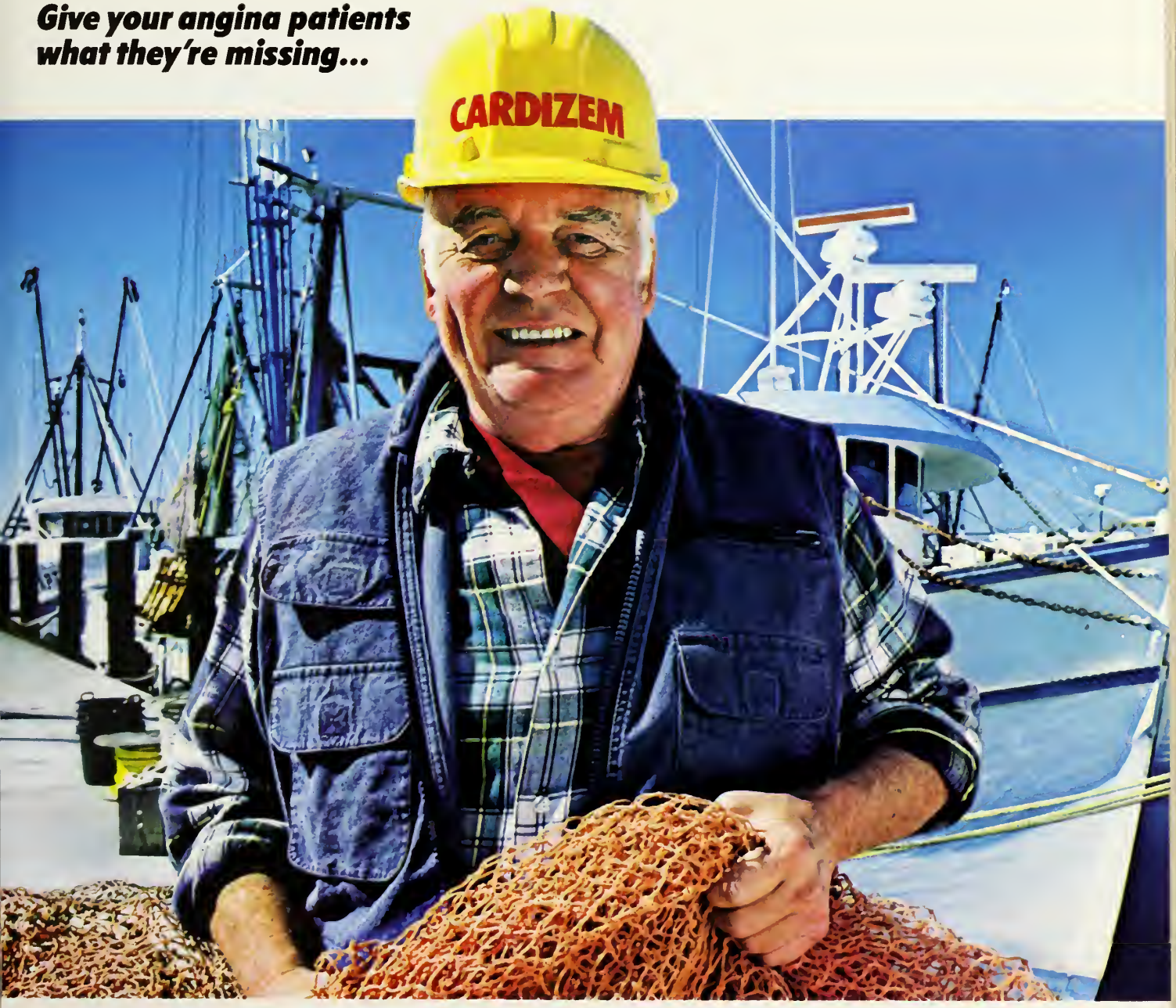
©1987, ELI LILLY AND COMPANY

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

700241

Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

Give your angina patients what they're missing...



CARDIZEM®: FEW SIDE EFFECTS

diltiazem HCl/Marion

- ***Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate***
- ***Proven efficacy when used alone in angina[1]***
- ***Compatible with other antianginals[2,3]****
- ***A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD[4,5]***

90 mg GREATER DOSAGE FLEXIBILITY NEW 120 mg

***See Warnings and Precautions.**

Please see brief summary of prescribing information on the next page.

CARDIZEM® diltiazem HCl/Marion

FEW SIDE EFFECTS IN ANTIANGINAL THERAPY

60 mg tid or qid

Brief Summary
Professional Use Information

CARDIZEM®
(diltiazem HCl)
30 mg, 60 mg, 90 mg, and 120 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV nodal refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.
Nervous System:	Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.
Gastrointestinal:	Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.
Dermatologic:	Petechiae, pruritus, photosensitivity, urticaria.
Other:	Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

Issued 9/86

See complete Professional Use Information before prescribing.

References: 1. Pepine CJ, Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with diltiazem, nifedipine, and verapamil. Am Heart J 1983; 106(6): 1341-1347. **2.** Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. Consultant 1984;24(Dec): 150-159. **3.** Johnston DL, Lesoway R, Human DP, et al: Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebo-controlled, double-blind, randomized, crossover study. Am J Cardiol 1985;55:680-687. **4.** Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. **5.** Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. Mod Med 1982;50(Sept):94-116.

Another potent benefit product from

PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC.
KANSAS CITY, MO 64137

1403E7

September 1987
Volume 70, Number 9

Rhode Island Medical Journal

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
OCT 1 1987

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903. Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℠

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

Volume 70, Number 9 September 1987

TABLE OF CONTENTS

395 **EDITORIAL**

175 Years Young

Seebert J. Goldowsky, MD

CONTRIBUTIONS

397 **A Discourse**

Read Before the Rhode Island Medical Society

Edmund T. Waring

401 **Discourse on the Object and Utility of the Rhode Island Medical Society**

Stat Nominis Umbra

409 **The Annual Address**

Before the Rhode Island Medical Society, June 13, 1912

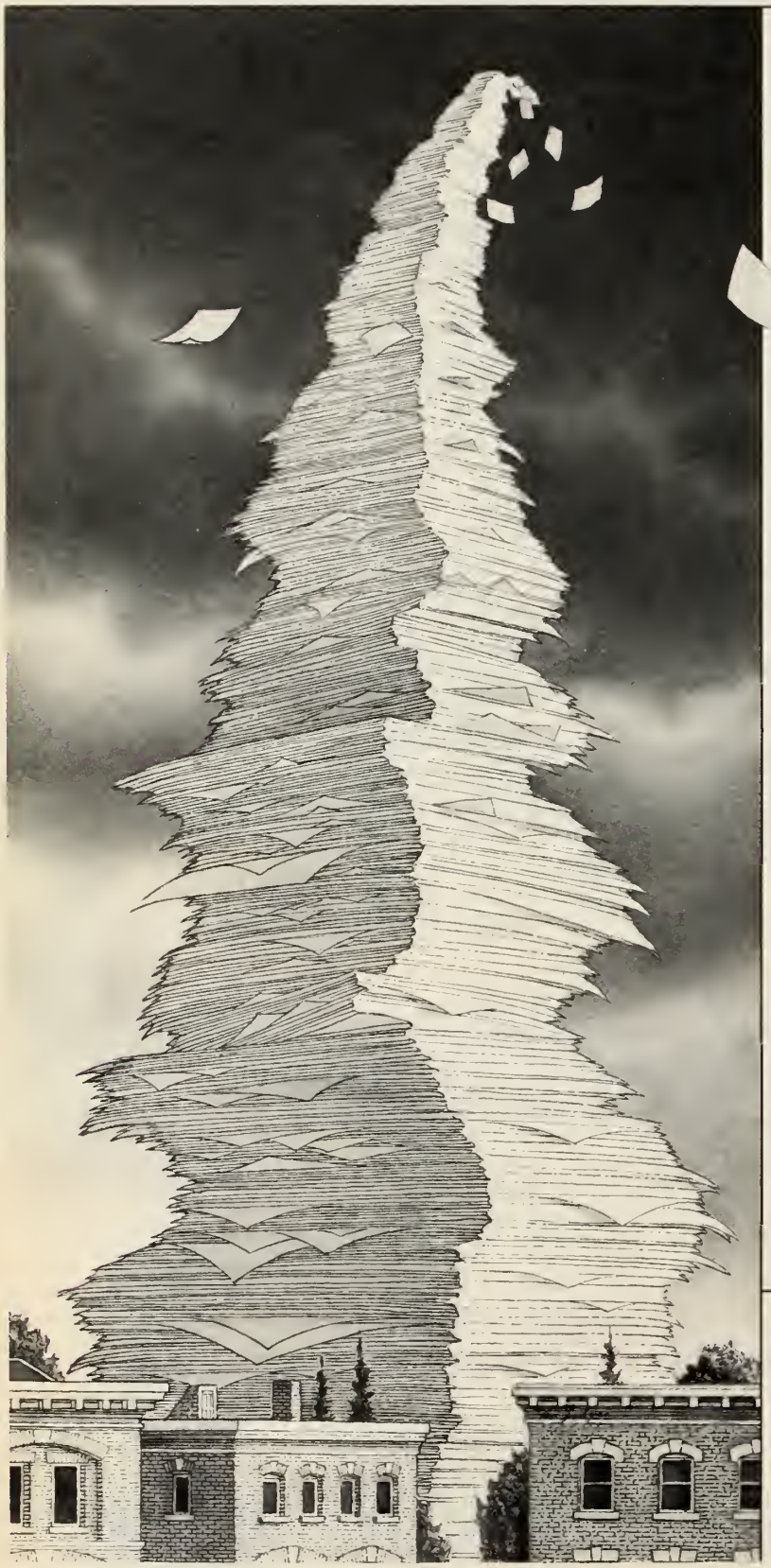
Frederick T. Rogers, MD

415 **The Doctor's Image — Past, President, and Future**

Samuel Adelson, MD

COVER: *The seal of the Rhode Island Medical Society. The present seal and motto was procured following a vote at the Quarterly Meeting in March 1888 authorizing Dr. G. D. Hersey to submit a new design.*

FINANCE YOUR INVESTMENTS WITHOUT INVESTING A LOT OF YOUR TIME.



When you've set your sights on a new medical office, computer system, or piece of real estate, your Private Banker at Bank of New England-Old Colony can make financing your investment as easy for you as writing a prescription.

No one understands your specialized needs and professional situation—and the way through the maze of tax laws, loan procedures, and red tape attendant with meeting your financing objectives—better than your Private Banker. Once your plan is in motion, this special banking relationship will continue to work to your benefit with ongoing timely and accurate financial counseling and direction. And our expert assistance is available to you without additional fees or extra charges of any kind.

With a responsive expert handling every detail of your financial requirements, you can continue doing what you do best without missing a beat.

Call Dick Boenning, Director of Private Banking, at 431-0100.

PRIVATE BANKING

BANK OF NEW ENGLAND
OLD COLONY

We take your financial goals personally.
Member FDIC

EDITORIAL

175 Years Young

The Rhode Island Medical Society received its charter from the Rhode Island General Assembly at its February session in 1812. An organizational meeting was called by Doctor Amos Throop for April 22, 1812 in the Senate Chamber of the old State House on Benefit Street in Providence. Throop became the first president. The first annual meeting was held on September 1, 1812 at the same location. Oddly, it was called the first "anniversary." As a result during the current 175th anniversary of the Society, it held its "176th anniversary meeting" this year.

This issue of the *Journal* commemorating the 175th anniversary of the Society is devoted to several anniversary discourses outlining the purposes and problems of the Society. The essay prepared for the 50th celebration, by Doctor David King of Newport, was never published due to domestic problems and the urgencies of the Civil War raging at the time.

We believe these interesting papers, varying greatly in style and content, will open a window on the problems of the profession at different periods in the Society's existence. The annual address of Doctor Peter D.T. Clarisse, read at the 175th anniversary celebration, was published in the August issue of this *Journal.* With a little foresight, it might have been contained herein for the purposes of symmetry.

We wish to thank Mrs. Helen DeJong, Librarian Emerita and an Honorary Member of the Society, now living in Florida, for proposing the concept on which this issue is based.

Seebert J. Goldowsky, MD

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY . . . . ANYWHERE

PLUS insurance for . . . .
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml *(1 teaspoonful)* contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg *(warning: may be habit forming)*; alcohol, 3.5 percent, in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

A Discourse

Read Before the Rhode Island Medical Society

Edmund T. Waring

In all ages and countries, the arts and sciences have maintained a distinguished consideration. Enlightening the mind and refining the heart of man, they furnish a scale of the progress of civilization. Signal have been the honours and privileges conferred upon their votaries. Tyranny itself has been abashed and bowed with reverence before them. By special mandate, the Philosopher of Syracuse was exempted from the sword of destruction, and a modern conquerour commanded his legions to pause when they approached the walls of Mantua, and himself paid homage at the tomb of Virgil. The reasons are obvious. They are formed in that law, whose authority all human nature acknowledges. The arts and sciences affect the dearest interests of man; they relieve his necessities, contribute to his comforts and safety, and gratify his ruling passions — avarice and ambition. The sciences in a special manner, elevate and ennoble him; they divest him of all that is sordid and mean in his nature; they incorporate all mankind into one family, cherishing the benignant and sublime principles of benevolence and love. For him the Botanist directs his steps to every clime; he leaves the cultivated plain and penetrates the deepest forests, where no human trace is found, to discover some new article with which he may enrich the natural history of plants. For him, the Chemist, with a scrutinizing and obtrusive spirit, not content with the mere externals of Nature's works, extorts from Nature's self, the secret of her operations, and by his inventive genius, forms a creation of his own. For him, the Astronomer, whose pursuits sublimate the mind, liberates himself from this spot of his abode, and ranges throughout the solar system. Directed by the laws of gravitation and repulsion, he determines the revolution of every planet, and unfolds the causes of our seasons; he guides the adventurous mariner through trackless oceans, and creates a social intercourse between the inhabitants of every clime. Winged by imagination, he o'erleaps the boundaries of discovered space, fancies other systems, and bows, at last, with religious awe, before the Great First Cause of the stupendous whole.

With sentiments of the most profound respect and veneration do we contemplate the distinguished character of the Physician. His subject is man himself — the last, the noblest work of God. For him, with feelings of the most refined philanthropy, he dedicates his life and labours — endures the inclemencies of every season — relinquishes the pleasures of social intercourse, and withholds from tired Nature the cordial of repose. Deplorable would be the state of man, unimproved by the Physician. Society would not exist — digust and self-preservation would annihilate the sublime principle of sympathy — man

This was read at the inaugural meeting of the Rhode Island Medical Society held in the Senate Chamber of the Providence Court House (which was also the State House when the General Assembly met in Providence) on September 1, 1812. The organizer of the Society and its first president was Doctor Amos Throop of Providence. Doctor Waring, chosen as Orator for the occasion, was a prominent Newport practitioner. The discourse was published as a pamphlet.

would flee from man — populous cities would be unknown, and mankind would be reduced to a level with the Arabs — wanderers of the deserts. That the science of medicine, which he professes, should render him respected and distinguished in society, is therefore natural. It is founded in the necessities and miseries of man.

This day, dedicated to the cause of medical science, demands that we should bestow on it our particular attention. We will cursorily consider its origin, its progress and improvements. Of all the sciences, that of medicine boasts of the highest antiquity. From the first introduction of disease, it existed, as is fabulously represented in the character of Hope, in the story of Pandora. The first evidences of its existence were furnished by the doubtful and hazardous experiments of distressed and sympathizing friends. Experience in course of events afforded some guide. This, which had afforded relief, was treasured up as a remedy; that which did not relieve, was discarded. But, it was not until the profession of physick was embraced that much progress in the healing art could be expected. Individuals devoting themselves exclusively to the observance of the symptoms, the progress and termination of diseases, and the effect of remedies, could alone advance it with any degree of certainty and usefulness. Ages, however, passed away without its being identified in the dignified form of a science. It lay imprisoned within the grasp of interested conjurers and imposters. At length a luminary arose in the person of HIPPOCRATES. Possessing a mind patient, acute and discriminating, he applied himself to the investigation of the causes, symptoms and varieties of disease, and was the first to promulgate the precepts of medicine. His discoveries and example excited a spirit of inquiry and emulation, which may be said to lay the foundation of the science. Greece deified him, and after his death, divine honours consecrated his memory. Unhappily, the dark and Gothick age soon succeeded. The science of medicine, with all the arts and refinements of antiquity, disappeared. A thousand years of medical history are distinguished only by almost continued marks of deletion. The few geniuses which appeared within that period were as meteors, evanescent and deepening the shade of the prevailing darkness. At length the night passed away. The few relicks which formed the monument of ancient greatness was collected, and a literary enthusiasm was excited. But the pride and indolence of man, impatient under the restrains of close investigation and experiment, soon indulged in theories; in supporting which, discord arrested the progress of improvement. The foundation which HIPPOCRATES had laid, was passed by, unheeded. Centuries rolled away, medicine was no more than a conjectural art; mankind continued the victims of pride of opinion. Again, the spirit of HIPPOCRATES revived in a BACON. To him mankind are indebted for the revival of all science, particularly that of medicine. He resumed the work which had been begun, and so long neglected. Not a Physician himself, he has given birth to thousands. Pursuing his instructions, a HERVEY discovered the circulation of the blood, which forms so important an era in the history of medicine. To him succeeded a SYDERHAM, than whom a greater genius never trod the path of medical science. He combated, successfully, the superstitious prejudices of society; introduced correct conceptions of diseases, and established a rational and successful treatment of them. From his time, we look forward to the present moment, with transports of joy and delight. A period less than two centuries, we observe, with enthusiastick admiration, a science rapidly advancing to a proud eminence. A galaxy of genius arose in Europe. A BOERHAAVE, a HALLER, a MUNRO, a CULLEN, a BROWN, a HUNTER, and a hosts of others, extended their lights to every quarter of the globe; diffusing health, happiness and life. Pursuing the course of rational investigation, Physicians adopted no theory, but what arose from facts and observations, established by experiment. They exacted tribute of all the arts and sciences. Anatomy and Physiology, Botany and Chemistry were united in promoting the interests of humanity. The human frame was critically examined; the functions of different organs, their relations, their sympathies and dependencies on each other were ascertained; the seat of diseases discovered; articles of diet and remedies for diseases multiplied, and the means of preserving health proclaimed. The terrour and consternation which pervaded families on the approach of disease are now supplanted by a grateful confidence in that faculty, whom they have seen restore limbs to the lame, hearing to the deaf, sight to the blind, speech to the dumb, reason to the insane, and even life to the supposed dead.

Gentlemen of the Medical Society of Rhode-Island,

From the conviction that medical science has been advanced by the united energies of individuals, you have laudably associated yourselves for its diffusion and improvement. As Physicians,

you have individually estimated the importance and dignity of the profession which you have embraced; you have realized the weighty responsibilities attached to it; you have been the guardians of the health and lives of your fellow-citizens. From the moment that man ushers into being, through the varying and perilous track of life, even to that solemn moment when Nature's mandate is to be obeyed, you have been his hope; the sympathizing colleague of the ministers of peace, to alleviate the agonies of death.

Great as your responsibilities have been, they are extended by your association. Heretofore you have acted as individuals; you are now clothed with the privileges of an act of incorporation: privileges which secure to you the right of authorizing and recommending Practitioners of medicine. Need I caution you in the exercise of them, against the indulgence of partiality or prejudice? Dreadful is the havock which ignorant pretenders spread on every side! Helpless widows and children, bereaved and disconsolate husbands, desolated families, are the sad trophies of their skill.

On you, your fellow-citizens will direct the eye of confidence. Voluntarily embracing the medical profession, with its additional privileges, they repose in you the guardianship of their dearest interests. Yours is the felicity to have the discoveries and experience of ages, descend to you by reversion. They are a legacy which it is your duty to preserve, improve and transmit to posterity. Great as they are, much remains to be done. There are still diseases which are the opprobria medicinæ. New diseases still arise within the circle of every man's practice. A recent discovery which has proved that a loathsome and mortal disease may be struck from the list of human evils, encourages the hope, that others may also be erased, by further investigation. Let not your successours reproach you with indolence; be animated by a noble emulation; cherish those liberal and enlightened principles, for which your profession has so long been distinguished; devote the talents you possess to the diffusion of medical science; and, when the evening of your days shall arrive, envied will be your retreat; gratitude will attend you with all her kind offices; reflection will preserve those sublime emotions which sprang from doing good, and self-approbation will brighten your future prospects with hope.

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue
Providence, R.I.
331-3996

120 Dudley Street
Providence, R.I.
331-3996

154 Waterman Street
Providence, R.I.
273-0450

38 Hamlet Avenue
Woonsocket, R.I.
766-4224

Discourse on the Object and Utility of the Rhode Island Medical Society

Stat Nominis Umbra

From the testimony of Antiquarians who occasionally come to us from the shades of those times which original monuments are fast ceasing to commemorate, we have reason to believe that mankind have never been presented with a more interesting age than the one in which we live. Never was learning more general; sense more common; reason more enlightened; society more refined; the arts more flourishing; and the sciences more diligently cultivated than at the present day. Geniuses are springing up in every direction, and are busily employed in the construction of fabricks to commemorate themselves to posterity. It seems as if human intelligence were beginning to acknowledge no bounds. Every old man is making some pretences to philosophy, and every old woman is ambitious to appear wise. Every house has its library; every library its readers; and every reader a competence of understanding. Boys and girls instead of being allowed to spend this interesting stage of their existence in trifling amusements and mental inanity, are compelled to rise with the first blushes of the morning, to shoulder their books, and trudge off to spend the day in the cloisters of literature. The brute rears his head, and appears anxious to change his fore legs into arms, and his tongue into a warbler of articulate sounds. The vegetable begins to blush, and cringe, and throw out its claims to instinct; and even the rocks themselves begin to creep, and exhibit signs of intelligence and docility.[1]

The Discourse was prepared by an anonymous author during the tenth year of the Society's existence. It was published as a pamphlet (February 1823).

Those, whose love for speculation has long led them to watch the motions of things in this incessantly changing world, are induced to believe that mankind have already fully attained to the Condorcet line of perfection. But this is far from the fact. It is freely acknowledged, however, that there is an immense difference between the state of mankind now, and what it was in the days of Galileo: when this distinguished Philosopher had the liberty of speech taken from him, because he asserted that the earth was spheroidal; and what it was, when Anaxagoras was confined in prison, because he insinuated that the moon was larger than all Peloponnesus: when the inhabitants of Jupiter were supposed to walk with their heads downwards; when the colour of the soul was said to be blue and its form triangular; when the sun was viewed as a huge rotundity of glass, and as emitting an unborrowed light; and when by many it was believed that the ebbing and flowing of the sea were owing to an immensely great fish, which breathed once in twelve hours.

But still there is room for improvement. Every day rolls along new inventions; new discoveries; and exhibits new gradations. Agriculture continues to advance, though it has been practised almost ever since our first Parents entered the garden Eden: nor has Philosophy yet done growing, though it has received the attention of a Newton, a Franklin, a Hally, a Kepler, a Montinaro, a Cavallo, and a Malpighi: and Divinity, although it has been hammered upon ever since the days of Plato, by geniuses the most consummate, and with an industry too which has known no bounds, still flourishes, and promises, under the aid of continued exertions, to exhibit new glories; new excellences; and new beauties. Influenced by

these encouragements, those who are looking for another, and better state of existence, are uniting and endeavouring in every possible way not merely to continue, but to multiply these exertions; and it seems as if they are determined not to stop, till they shall have exhibited to the world the dignified science, in the last degrees of perfection.

They have formed themselves into societies, and are poring over the pages of ancient and modern literature, to give impossibility to failure in their glorious enterprize.

But Divinity is not the only science, for the sake of cultivating which, mankind have seen fit to combine their exertions. Societies have been established in various parts of the world to advance, and bring to perfection, the science of Jurisprudence. A premium of fifty louis was not long since granted to M. Hongard, of Switzerland, for the best dissertation on this question: "Would the institution of Juries in criminal cases prove advantageous in the Canton de Vaud."

Societies have been formed for improvement in Musick; to invent new strains; to discover new beauties in the art; and to bring to the ear the charms of united voices in all their endless varieties of harmony.

Societies have been formed to aid the progress of Mineralogy; to trace the caverns, and explore the bowels of the earth, and to bring to light the hidden beauties and treasures of nature.

To give advancement to a science, it is necessary that those, whose wish and object it is to see it advanced, should bring their exertions together. By the united exertions of a few, that may be accomplished in a short time, the doing of which would require an everlasting age of individual toil and hardship.

In this state, a society has been formed, denominated the "Rhode Island Medical Society."

Frequent inquiries are made, What is the object? And what is the benefit of this society?

Those who have cultivated their understandings, and have become acquainted with the scenery of Parnassus; who have turned from the abodes of superstitious ignorance to wander in the "primrose paths of literature," are not ignorant of the object, nor are under the necessity of inquiring, Where is the benefit? Or in what consists the utility of this society? — Those whose poverty in some instances, and whose mental torpidity in others, has kept them from rising in the world to behold the wisdom and operations of a refined and enlightened community, are the ones who so frequently make these inquiries, and for whom this discourse is principally designed, and to whose benefit it is humbly consecrated.

Their attention, therefore, is invited in the first place, to what is said as touching the object of the society:

In the second place to what is offered in regard to its utility:

And in the third place, to such remarks as necessarily grow out of the subject.

I. As touching the object of the society.

The object of the society every wise man will pronounce to be good.

1. It is to preserve among all its members a strict uniformity in regard to charges for all Professional visits and Medical prescriptions; to prevent any one from offering to prescribe without compensation; from manifesting a dog-tail[2] obsequiousness to him who carries in his countenance the symptoms of an approaching malady; from lurking about the residence of a sick person, who is attended by another Physician; and from practising, in any way, manner or shape, underhanded and dishonest means by which to obtain more business than another.

2. To get skeletons in order to ascertain the nature, constitution, and endless intricacies of the human body; and so far as it comes within the limits of possibility, to discover the connexion between matter and mind, and in what the one is influenced by the other; and to find out, if it can be done, what diet, and what habits of living are best calculated, to keep the soul and body together.

3. To foster the growth of Chirurgical and Pharmaceutical science; to perfect the practice of Medicine, and to bring under its control, the Proteus-like, deceptive and multiplying diseases of the day; or otherwise, to shut the box of Pandora, and restore to the pining inhabitants of this pestilential world, the blessings of gigantick[3] bulk and the ineffable glories of antideluvian longevity.

4. To arrest the progress of quackery, that hideous monster, whose head like the Hydra's, has hitherto multipled by amputation; whose liver, like Prometheus' has grown as fast as it has been devoured; and whose strength, like Anteus' has increased under subjugation: a monster which has navigated every sea; mingled its breath with every breeze; reared its head in every clime; and, ever since the days of Hippocrates, been traversing the earth, and peopleing it with corpses: or otherwise, that unprincipled wight, that vain pretender to the art of healing, who has lived long; obtained celebrity; and in whose veins the

blood still circulates, though meteors have burst o'er his head, and the earth quaked beneath his feet, though streams of lightning have pursued him behind, and the thunder of opposition has met him before: a being, who, if suffered to exist, to use the lancet and administer his nostrums, will soon extinguish the whole human family, and convert the earth into a wilderness, to which the light and heat of the sun will be transmitted to no purpose; where the tempest will roar, the brooks murmur, and the birds sing, without being heard by the ear of intelligence; where the dews of the morning will soften skin, and whiten the cheek of no beauty; and where vegetation will flourish in vain.

II. It is now proposed to offer something in regard to the utility of the society. And here, to use an expression of the great Roman orator, speaking of the character of Pompey, *it will be more difficult to find out where to stop, than how to begin.*[4] To enumerate all the benefits which have resulted from the establishment of this society, would be distracting to the writer as well as tedious to the reader. It is therefore intended to be as brief as the nature of the subject will admit, and yet, to be as comprehensive as possible.

1. Since the establishment of the society a number of diseases have changed their character: that is, have become less malignant, and are more easily managed. They visit us less frequently; excite less alarm and seem willing to acknowledge that it is in vain to contend against the formidable sons of Esculapius. The writer of this discourse does not recollect that there has been an instance of the Small Pox within the limits of the state, for more than eight years; and he knows, that during the same time, it has not been at all common for grown people, to be brought down with Measles, Mumps, or Whooping-cough. The plague, which, in the year 1665, swept off so many of the inhabitants, of London; which bid defiance to every Medical restraint; which ravaged every part of the city, and selected its victims from every house, has known no existence in this state, since the establishment of the Medical Society. The Typhus Gravior has been brought down to Typhus Mitior; and the Spotted Fever has been stripped of nearly all its malignity. Other diseases have altered — but the changes are too numerous to be given in detail. Consumptions remain about the same. Instances of the Yellow Fever are seldom.

But, says the objector, "Is not this change in the character of diseases to be attributed to changes in the state of the atmosphere? How can the Medical Society change the *real character* of diseases? Admit that the Dysentery and Cholera-morbus raged less, and attacked with less violence, last year, than they did the year before. What reason shall be offered for it? Was it in consequence of some influence which the Medical Society exerted over them? If the mildness with which they made their appearance the last year, is to be imputed to the Medical Society, show me the grounds of the imputation. I do not understand it."

Although these interrogations, when fairly analysed, amount to but little; still as they are frequently thrown out with an air of contempt and reproach; it will not, it is hoped, operate unfavourably, or be attended with any melancholy sacrifice of dignity to answer them.

All that the Medical Society can do, and, if the writer is not mistaken, all that they profess to be *able* to do, is merely to remove the originating causes of diseases. Stagnant water, and putrified vegetable matter originate what is called the Yellow Fever. It is practicable, in many instances, to remove these causes of this malignant disease, as well as those of many others; and in *this* sense to change their character. Is not this intelligible?

But the objector again says, "I cannot see how the character of a disease is changed by removing its originating cause. It appears to me that this is not talking philosophically." In reply to this, but one remark is necessary; and as the subject is too abstruse to be treated of in ordinary language, it will therefore be given in the Medical dialect. "Tityre, tu patulae recubans sub tegmine fagi."

2. The society has had a tendency to make more competent and more skilful Physicians. The laws of the Society require that every candidate shall have studied, at least, two years, and have become familiar with the contents of such and such books before he can be admitted to legal practice. He is examined by the Censors, and if qualified, is by them approbated, and recommended to the publick as a regularly educated Physician.

In consequence of these regulations, those only at this time, attempt the study of Medicine, who are, as Hyppocrates says they should be, possessed of geniuses adapted to the art; who have received from nature an exquisite discernment, a sound judgment, and a character which exhibits mildness, firmness and generosity; who suffer with the sufferings of others, and who feel commiseration for the woes, that are incident to

human life.[5]

Till within a few years, Physicians have many of them, like mushrooms, sprung up *improviso,* and come to maturity in a few hours. They have laid down the smooth-plane, one day, and taken up the lancet the next: have gone from the slaughter-house, at evening and awakened Surgeons in the morning; and from venders of tea cups, have instantaneously transformed themselves into Doctors of Medicine. So far as the Medical Society has had a tendency to prevent such unnatural transformations, so far it must, by every candid and enlightened mind, be acknowledged to have been of great utility. The merits of learned and skilful Physicians have been too long concealed. Through the influence of this Society, they at last begin to appear. The world begins to acknowledge that the necessary qualifications for the practice of Medicine are not to be obtained in a day; and that men of weak judgment, and ordinary information, are not to be trusted with the lancet, the glyster-pipe and the squirt-gun. The publick have long enough witnessed the evil effects which have arisen from the application of these things by those who have never been initiated into the arcana of Medicine.

3. The establishment of this Society has a tendency to advance the knowledge, extend the usefulness, and enhance the dignity of its members. Agreeably to the regulations of the Society, one of its members delivers at every annual meeting, an essay, commonly called an oration, on some disease which is common to the climate, in which he gives an explanation of its nature; shows under what circumstances it attacks; and what is the best way in which it is to be treated. These essays are commonly very interesting; very instructive; and very useful. Unborn generations do not yet know how many benefits are going to accrue to them from the establishment of this Society.

O, ye not-yet-created beings![6] permit me to give you a hint to be preparing, ere entity overtake you, to receive them with gratitude, and to use them as not abusing them. Be preparing, I say. Have ye never heard the old adage, that the wheel of time rolls rapidly? Be entreated then to be preparing: for your birth; yea, your birth is drawing upon you after the rate of three hundred and sixty-five days to the year.

4. Since the establishment of this Society, the subsistence of those who compose it has become, in a considerable degree, less precarious. Being united together in one common body, they seem, however different it may have been before, to have acquired a kind of equilibrium, if I may so speak, of respectability. It is not unphilosophical to suppose that they should. Let divers bodies, possessing different degrees of warmth, be brought within the vicinity of each other, and in a little while, they will all acquire the same temperature. One will be as warm as the other. Let it be understood, however, that if the atmosphere around is hostile to heat, warmth will very soon depart from the whole, and they will all be equally cold. Since then the members of the Society are all equally respectable, the publick are not under the necessity of going though a painful process of discrimination to know whom they shall employ to rid them of their maladies, but commonly call in the one who is most handy. Hence all have nearly the same amount of practice; are all equally prosperous; equally rich; equally useful; and equally distinguished. All charge alike; prescribe alike; think alike; and act alike: respect each other; counsel each other; and uphold each other. Upon the merits of such a state of things as this, there needs be no comment.

III. It is now proposed to close the discourse with a few remarks.

I. From what has been said, it appears that there have been *good reasons* for the establishment of this Society. Objections, it is well known, have been raised against it. The finger of contempt has been pointed at it. The reproaches of the ignorant have been vomited upon it; and the venom of empiricks has been aimed at its vitals. Its members have been accused of illiberality; and of being excessively dear in their charges. — As sickness diminishes, and business grows less, the value of practice will of course be enhanced. Under such circumstances, it becomes necessary to charge higher, in order to obtain support. But they are also accused of having come to an agreement to charge so much for such and such services. Be it so: And what impropriety is there in this? Is not the justice of such regulations sanctioned by what we see in those of *other* professions — among fellow craftsmen of different denominations every day? Did not the wood-sawyers, a few weeks since hold a publick meeting on the bridge in this town,[7] and resolve that whoever of their number should saw wood for less than eight cents a foot, should forfeit both saw and horse; yield them up for publick auction, and have the avails of them laid out in rum for the benefit of the Corporation.

Again, Have not the oyster-venders, whose stand is a little north of the Fish-Market, always been uniform in their prices? — that is, is not a dish of oysters to be had from one, as cheap as

from another? And have not these comely citizens spent whole hours in profound legislation, in order that no one may undersell and by this means obtain more custom than another? Once more, Where shall we go to find a more uniform and systematick course of dealing, than that which is practised among our Candy-boys? Notwithstanding that diversity of character and disposition which exists among these youths, and the thousand temptations to which they are exposed to become unfaithful; yet — How perfectly true are they to each other? Who ever gave more, or bought for less than a cent a stick?

2. From what has been said, it appears that Medical science is fast improving, and every day increasing in dignity. Through the influence of societies, it has attained to a degree of perfection which the most unbridled enthusiasts never anticipated. Through the same influence, also, Physicians have become more respectable, and infinitely more useful. Owing to the same influence, also, have not diseases begun to change their character? Have they not become less deformed — less malignant, and are they not less mysterious in their operations? Let the reader answer for himself. Was not the character of diseases changed in the days of Esculapius? Did not this distinguished Physician raise Hyppolitus from the dead? And did not Jupiter strike him with lightning, because Pluto complained that he had been the means of depopulating his Empire, and of diminishing his revenue?[8]

But what shall be said of Quackery? Has not the Medical Society under consideration, had some tendency to suppress it? Unquestionably. Still it has not done it effectually, and never will without the aid of government. The subject ought long since to have been brought before our State Legislature. The Police of Paris, from a conviction of the mischief and damages resulting from the secret remedies of Charletans, have recently revived and enforced with double rigour the law which prohibits the editors of journals and newspapers from publishing the advertisements of quacks and pretenders.

3. From what has been said, how excellent, how exalted, how dignified does our Medical Society appear? Where shall we go to find an institution which reflects more honour upon its founders, or has been more liberal in its benefits to mankind? Societies are numerous it is well known. Almost every occupation — almost every sort of business has a society to advance its interests and clothe it with dignity. Many of them are useful, and seem entitled to existence. Among those of this character, not only our own, but Medical Societies generally ought to be classed. Good were it for the world, were there ten of these societies to where there is one. The writer feels thankful, however, that he has it in his power to say that they are fast increasing. At Paris, in the year 1820, a society was formed, denominated the "Royal Medical Society of France." It is under the patronage of the king; has gone into operation; and has been promised the support of all the grandees of the nation. Let the spirit of improvement which now reigns amongst men continue but a few years longer, and the light of Medical Science will dawn upon every land, and diffuse its blessings throughout the world. Societies for its promotion will spring up in every direction, and the cry of its utility will ring from Greenland to New-Holland; from Kamptschatka to Peru.

Footnotes

[1] In the American Journal of Science and Arts, Vol. 5th, page 34th, edited by Professor Silliman, is an interesting account of moving rocks, in the town of Salisbury, Conn. They are situated in a small lake, not far from a publick road; and, for a number of years, have been known to creep upwards of three feet, in eighteen months.

[2] Everyone knows the deportment of the dog, when in want of favours from his master. This adjective, therefore, it will be perceived, gives to the word "obsequiousness," a very wonderful *impetus*. As the expression is pithy and full of meaning, the author believes that it will, notwithstanding it is low, meet with the approbation of the reader.

[3] There were giants in the earth in those days. Gen. vi. 4. What the size of these giants was, we are not informed. Moses knew, doubtless; but he did not see fit to give us a description of them. Probably there were somewhere about the size of the Cyclopes or

There are three ways to bi

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
#
#
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj	CURRENT BALANCE
		BALANCE FORWARD →				60.-
8/30/85	James	Bal. Forward				60.-
9/3/85	" "	O.V	40.-	Billed 9/5/85		100.-
9/30/85	Medicare pmt/adj.			-45.-	-8.-	47.-
10/10/85	patient pmt.			-7.-		40.-
10/25/85	Medicare pmt/adj.			-28.-	-5.-	7.-
11/10/85	Pt pmt.			-7.-		-0-
11/20/85	James	Int O.V	40.-	Billed 11/21/85		40.-
12/5/85	James	Surgery	300.-	Billed 12/20/85		340.-
1/5/86	Medicare pmt/adj			-28.-	-5.-	307.-
1/17/86		Coins. adj.			-3.-	304.-
2/2/86	Medicare pmt/adj			440.-	250.-	114.-

PLEASE PAY LAST AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp. Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

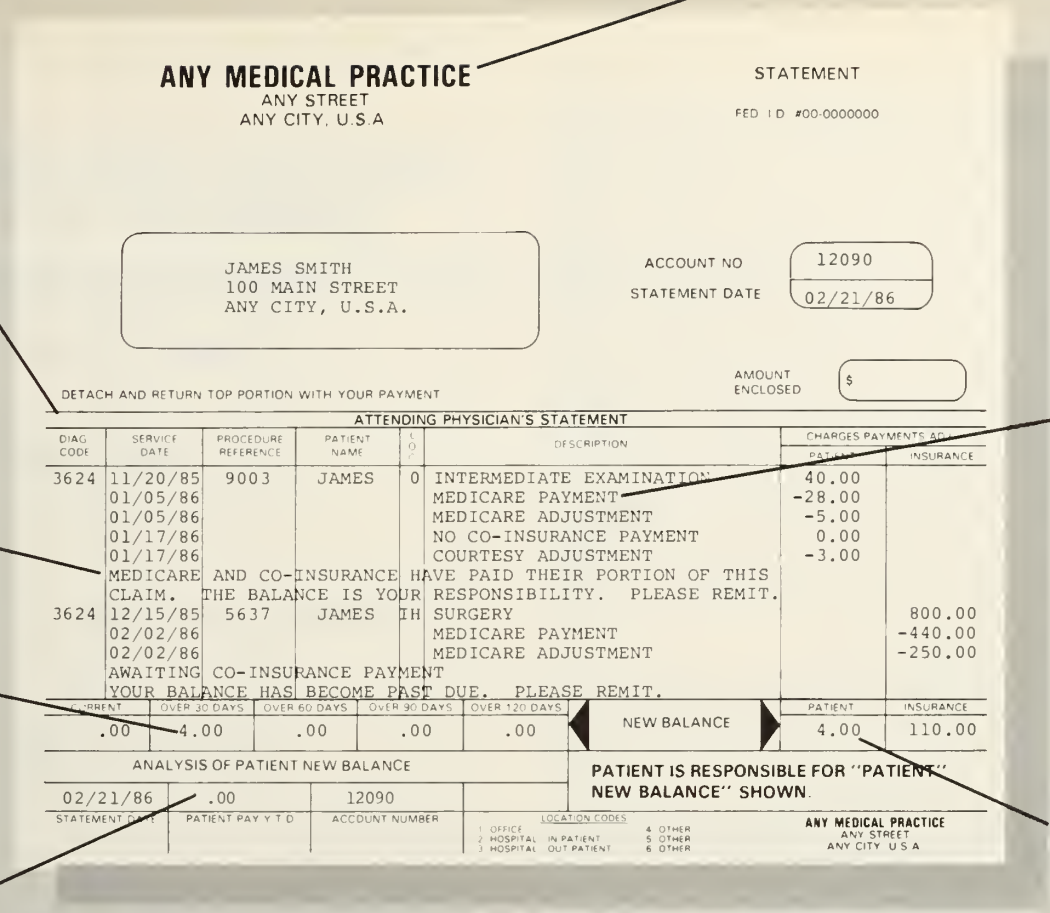
BILLED FROM 1-21-86
BILLED TO 2-20-86
DATE 2/21/86
ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

our patients.



THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices

Cyclopses — a race of beings, of whom we have an account in Virgils' Æneid, book 3. This author gives a particular account of one of them, named Polyphemus, and of the injury he received from Ulysses. The eye of Polyphemus, for he had but one, and that, in the centre of his forehead, is represented by Virgil to have been about the size of the sun's disk: "Phoebeæ lampadis instar," book 3, line 637. "Trunca manum," says he, in line 657, "Trunca manum pinus regit, et vestigia firmat:" i.e. The trunk of a pine tree supports his hand, and makes his footsteps firm. His hand must have been about three feet in length, and his height more than twice that of ordinary pines. The pine is one of the tallest of trees. We have a better idea of his height from the following: line 664, "Graditurq; per equor jam medium, necdum fluctus latera ardua tinxit:" i.e. "And while he stalks through the middle of the sea, the waves do not *even* tinge, that is do not come up to his lofty sides. His body was probably thirty feet in diameter, and his height considerably more than that of the steeple to the Rev. Mr. Edes' Meetinghouse. The giants of the Old World were in all probability about this size. What genteel forms they were? What a blessing it would be to possess such a bulk? What journies could we not take? What enterprises could we not accomplish?

[4] Dicendum est enim de Cn. Pompeii singulari eximiaque virtute: hujus autem orationis difficilius est exitium, quam principium invenire.

[5] Abridgement of Anacharsis, p. 457.

[6] The author is not ignorant that this is a contradiction in terms. He was compelled, however, to adopt the expression from the penury of our language. He could see no other way in which to being the apostrophe than this; "O, ye not-yet-created beings;" that is, those who have not yet begun to exist; but who, at some future period will, *scrie volvente annorum.*

[7] Providence.

[8] Tooke's Pantheon, page 270: also, Virgils' Æneid, book 7; and Lucian's Dialogues, page 50, of Graeca Minora.

MEDICAL SUITE AVAILABLE FOR RENT

1240 square feet
ample parking

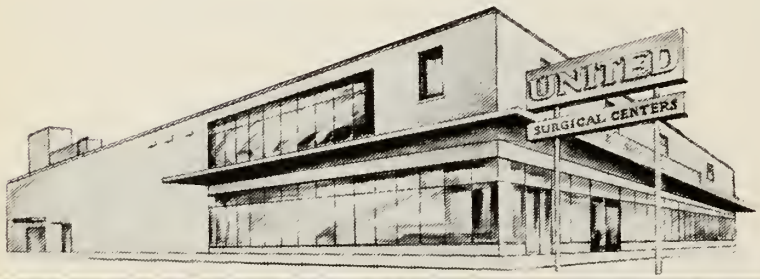
Barrington Medical Center
East Providence

Call 433-2400

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

The Annual Address

Before the Rhode Island Medical Society, June 13, 1912

Frederick T. Rogers, MD

If one attempted to enumerate the problems in medicine which have been solved during the century of existence of the Rhode Island Medical Society, the task would be stupendous; equally difficult would be the endeavor to consider the problems which in all probability will be solved during the next hundred years, and although sadly handicapped by the limitations of time and lack of ability in the fulfillment of the duty which devolves upon me as President of the Society, I desire to call to your attention one problem which confronts us at the beginning of a new century of medical progress. This is not concerned with the ravages of tuberculosis, the etiology of cancer, the spread or prevention of communicable diseases, nor with any of the usual manifestations of activity in the medical world to-day, but a problem which, if appreciated and considered in a purely impersonal manner, is of equal importance, for upon it largely depends the successful outcome of all the other tasks set for us.

How shall we regain the respect and feeling of security and confidence in the medical profession which was such a strong factor in human life a hundred years ago, but which now is unfortunately lacking?

Reprinted from the Transactions of the Rhode Island Medical Society *8: 265-273, 1912. This was the 100th Anniversary of the Society. Doctor Rogers was a prominent otorhinolaryngologist.*

There was a time when the minister, the squire and the doctor were a power in a community with none to dispute their position. That all have suffered in the lapse of years is evident, but we are most concerned with that which has lowered our own profession to a condition of competition with interests which are not influenced by the ideals which have always governed the practitioner of medicine.

Am I pessimistic, do I exaggerate, or do I need to adduce proof of this premise? Recall the vicious attacks of the antivivisectionists and the antivaccinationists, the slanderous statements of the crazy cults which would do away with all diseases by declaring them non-existent, and the thousand forms of quackery which thrive by discrediting our actions. Read the daily newspaper which admits to its advertising and pure reading absolute falsehoods and preposterous claims inimical to the profession, and the Comic Weekly, God save the mark, which holds us up to ridicule. In a crowded assembly, cry "Doctor," and see the osteopath, the optometrist, the veterinary, the chiropodist, the masseur, all start from their seats, and then tell me the title of Doctor is synonymous with what it once did and what is should now represent.

No longer is the physician as he was a hundred years ago restricted in his field of action to the relief of suffering and the cure of disease, for the art and science of medicine is more and more communal and less and less individual, and today it deals in the broadest sense with the welfare

of future generations as well as of the present. Treatment and prophylaxis are no more essential than hygiene, education and rational living, and the propaganda of health is our sphere of action rather than any school or "ism."

"A house divided against itself cannot stand." So the energies of the medical profession badly directed in a hundred divergent ways must fail of an ultimate accomplishment readily acquired by concerted and uniform action, and before we can attack any evil which menaces the profession from without we must be sure of our own defenses, that no criticism we make of others should have elastic properties and rebound to our own discredit. When we can lift our profession above the plane of commercialism, when we can conduct ourselves without petty squabbles of medical politics, of schools and isms, without personal animosities, when we can do away with the evils of fee-splitting, when we are not open to the charge of hasty and ill-advised operations, of faulty and incorrect diagnosis for personal gain, then may we begin the fight against the forces which are a menace to public health, and with their downfall and our own consequent betterment once more attain our former position as chief of the learned professions, once more acquire the confidence of the public and again rejoice in the fact that the act and opinion of the true physician is always in the interests of humanity, never in self-interest and none may gainsay his motives or question his integrity.

That our defenses are weak and unable to withstand attack is unfortunately true. We decry commercialism, yet succumb to its exigencies, and perhaps no more glaring illustration of this fault can be found than the position unwittingly assumed by the profession in regard to one operation. The presence of adenoid vegetation in the naso-pharyngeal vault presents a clinical picture unmistakable to the physician and their removal assures certain definite relief, but the subject has received so much attention in the popular press, so many write-ups in the current magazines and has been so widely advertised by the results of the medical inspection of schools that the laity is assuming it ability to diagnose this condition, and daily there appear at our clinics parents who do not desire to know if their children have adenoids, but who plainly state that they wish them removed. The duty and privilege of the physician to diagnose and prescribe for an ailment as his judgment dictates is completely ignored, and he is asked to prostitute his calling by exercising only manual skill at the bid of a layman. It is no unusual occurrence at the hospitals in this city for the surgeon to operate on fifteen to twenty cases in an hour or two exactly as he might go out before breakfast and hoe fifteen or twenty rows of corn, and the effect of such reprehensible action is to impress the laity with the idea that the operation is a mere trifle devoid of danger, requiring no particular skill because no particular pains are taken. The operation for adenoids has become a commercial factor in our life and is subject to the usual market fluctuations. Every day some one telephones, "How much do you charge for adenoids?" exactly as they telephone to the market to ask the price of pork, and so they go the rounds, seeking for a bargain sale of adenoids till the lowest bidder gets the job irrespective of the nature of the case or the need of the patient. No wonder that the apparently simple operation is sometimes barren of results, sometimes marred by disaster. Nor is it a wonder that the public consider it to be a trifle requiring no more thought than a visit to the manicure. The same is true in a lesser degree of many other operations. The surgeon is approached not by a patient, for sometimes no opportunity is given for examination and diagnosis, but by a customer, who calmly asks the price for removing an appendix, or an ovary, curetting a uterus or extirpating a supposed cancer. As a result not a few healthy appendages and normal tissues have been added to the collection of the irresponsible surgeon.

Operative skill should not be affected by the exigencies of competition. The honorarium demanded should be commensurate with the responsibility assumed and the skill and training required, and there should be neither fee-splitting nor fee-cutting. Rather should there be occasional gratuitous service when such is not required than that we should belittle ourselves by asking for our services fees inadequately commensurate with the dignity of the profession. These are but examples of an evident fact. Professional services are often measured not by ability, nor by skill or experience, but by price, and many a man owes his popularity and present lucrative practice to the fact that at one time he offered his services at bargain prices. A man should not attempt to do a thing until assured in his own mind that he can do it as well as any and better than most, and he should not then belittle his own effort by demanding an insignificant fee.

Not long ago a patient consulted me for what I thought was a tuberculous laryngitis, an opinion with which her physician did not agree, and

after listening to our discussion the patient said: "Well, so far as I can see, if I want to know if I have consumption I shall have to go to the Society for the Prevention of Tuberculosis and let them decide it." The patient really believed that the society with the long name was a court of last resort in pulmonary disease and the physician a mere adjunct.

It is because of our inaction, indeed our culpable negligence, that there has arisen the necessity of forming the various societies for the prevention of this and the suppression of that, the District Nursing Corps and the hundreds of similar associations for the relief and care of the sick, all founded by laymen, governed by laymen, usurping what should be the prerogative and privilege of the profession, and doing to-day what we should have done years ago. That this opinion is shared by the laity is evidenced by a recent article in Science, which says: "Many of the worst evils of our present-day civilization, dirt, ill health, despondency, pauperism and crime, are a large part due to the failure on the part of the majority of those trained in medicine to act as leaders and public educators. Health of body and mind should be recognized as of first importance to the community." "They have been so recognized, so far as they have been understood," says Havelock Ellis, "in every great period of civilization of which we have much knowledge, as Roman and Moorish ruins alone suffice to testify. That they are not so recognized to-day is the chief element of rottenness in our civilization. We postpone laying the foundation of our social structure in order to elaborate its pinnacles. We have not yet learned that a great civilization is ill built up on the bodies of men and women enfeebled and distorted by overwork, filth and disease."

We are too exclusive and the public knows little of the real workings of medical life. Occasionally, it is true, the daily paper reports that Dr. A. is attending Mr. B., and more frequently it records the fact that Dr. C. was arrested for speeding his automobile, but we have always been proud of the fact that we did not advertise our calling. The fact is that when we do advertise ourselves it is usually to our discredit.

Every now and then one of our medical societies sends a committee to oppose some inimical legislation, such as granting a commission for the optometrist, and very recently for the osteopaths, and the papers record this fact. Very infrequently we read that the State Board of Health has attempted to have some poor wight arrested for practicing without a license, and so far as results are concerned this meagre notice is all we gain, while every day and hundreds of times every day through the public press there is exploited to the lay reader, men and means of immeasurably greater menace to the public health than could be ascribed to either the optometrist, the osteopath or the illegal practitioner, and we sit idly by with no thought of remonstrance, and when we do consent to take our valuable time to oppose such legislation, at once there arises a cry of protection of medical interests, and our efforts are vilified and held up to ridicule. It serves us right. This is not the way to deal with the problem. The optometrist wanted a commission and we vigorously but ineffectually opposed it, and now that they have it no one knows what they have done with it, and I do not know of any harm it has done the public. What we should do rather is to devote our energies to the public itself, educate them, and teach and show them the fallacies of these claims for the impossible.

Just as the press has been the means by which the enemy has entered our camp, so must it be the power by which we shall expel it, and the incongruity of sound medical advice in one column while dangerous and criminal quackery rages rampant in another should be met by us with reason, with facts and with equal publicity. The medical profession has too much to do to take up a defense against quackery; its services are too valuable to be so wasted, and it should be so guarded and protected by the State and so aided and encouraged by the public press that the mere ability to practice medicine within the law should be a guarantee of competence and integrity. Lack of such aid degrades the highest service to humanity to a struggle for existence, and those who survive are not always the fittest.

Fifty years ago this State spent in one year for all purposes dealing with the public health a few hundred dollars; last year it spent $172,727. The various hospitals in Providence expended over $350,000, five municipalities spent $200,000, and if we consider the various allied dispensaries, societies and associations, not less than $800,000 was expended in the year 1911 for the relief of suffering and the prevention of disease. To this must be added the enormous amount of charitable work done independently by the profession with no thought or expectation of pecuniary reward, and all this in a State which has a population of less than 600,000. Either we live in a community of medical paupers or we are approaching an era of paternalism in medicine. During this same fifty years the mortality of ty-

phoid fever has been reduced from 4.2 to 0.8; scarlet fever from 5.2 to 0.4; diphtheria from 2.5 to 1.2; and tuberculosis from 17.6 to 11.5. Does any one believe that this result has been attained by the expenditure of mere money? On the contrary, it is the life blood of the profession which has been shed and is the result of unceasing effort to advance the science of medicine. It represents years of toil and research; thousands of lives have been sacrificed to make it possible and the gain to the State, thje longer life granted to us has been made possible only by the lives and services of the medical profession. But if we ask the average man how these results have been gained, he will say that they are due to the paternal efforts of the State, that the advantages accruing to posterity by the better care of our children are due to wise legislation which inaugurated school inspection, to the hospitals which care for the sick, but to our profession, without whose aid and service none of these benefits would accrue, little credit is given. The tendency rather is to discredit both our actions and our motives.

The relation of the profession to medical institutions has not yet reached an equitable adjustment. Those who are not associated with the hospital decry the unfair advantage held by the members of the staff, while those who do the hospital work make loud outcry against the injustice which compels them to treat gratuitously patients abundantly able to pay for professional skill. Hospital abuse is still with us and is not confined to that one feature of ill-directed charity which permits the well-to-do to visit our dispensaries, and which a few years ago allowed free service in one year to people of this city who were taxed for nearly a million dollars of real and personal property. It has invaded the profession, and the hospital surgeon who declaims the loudest against the injustice of allowing the wealthy patient in the private ward is perhaps the one who takes his own wealthy patient to the hospital for a free expert opinion and his fractures to the same economical place for this X-ray work, who takes his own family to the oculist and sends his patients to the optician, who treats his gynecological cases till their patience is on an equality with their resources, and then refers them to the hospital. Sad to admit, there are those of us who do these shameful things ignorant of the fact that our motives are perfectly evident to the public, and that their opinion of the profession is lowered by just that much.

It is much easier to sound encomiums upon the profession in resounding phrases, to speak of the high ideals which should govern our lives and of the progress made and successes scored during the century, and it is with no spirit of fault finding or carping criticism that I am obliged to admit the existence of these conditions. Our skirts are not clean, and until we can down these evils which menace our profession, we should not expect to be held in the honor and esteem which were the inheritance of our forefathers in this Society.

A remedy for these evils, which I have taken so much time to describe, is, I believe, at hand, and, purged of its faults, the medical profession will by its very inherent strength rise again to the proud position of leader amongst the learned professions, and the weapons are organization and publicity. We must avail ourselves of modern armament in a warfare to-day. This is no medieval battle to be waged, and the same methods which prove of service to our enemies must be utilized by us. The labor union, the grange, the successful business, the great corporations, the dominant political party are all the result of organization, and in the national association, the State and district societies we have all the elements of a similar successful campaign. These should be and can be made of so much value that the medical man cannot afford to be without the pale of membership. The test of ability and integrity should not be, "Is he a graduate of this college or associated with that hospital?" but "Is he a member of the State Society?" Our antiquated methods should be consigned to oblivion, old fogyism relegated to ancient history, and we should emerge from the seclusion and exclusiveness which has been a source of pride and a cause of weakness and get into the limelight of publicity, leaders in everything pertaining to public health, not followers or hangers on, but leaders, prominent in the warfare against disease, active in the counsels of philanthropy and charity, outspoken in questions of civic probity. These are the attributes of a medical profession which stands for all that its name implies, all that its history demands. The scope of this Society should not be the reading of papers with perfunctory discussion, should not be the annual banquet or quarterly collation, nor the publication of transactions which nobody reads, but it should actively concern itself with the problems of life about us. It should have opinions and express them boldly, assuming that no one has a better knowledge or a better right to guard the public warfare. Committees on legislation are an-

tiquated and useless. They have accomplished nothing in this State and almost as much in others. Legislators do as they are told, and with the orders of the boss ringing in their ears they can scarcely hear the whisperings of conscience, much less the softer murmur of the Committee on Legislation. The osteopathic bill before the present Legislature has blazed the way for future bills of like character by employing a lawyer to draw the bill, whose fee is large enough to include his services as political boss, to force it through legislative channels. Our breath is wasted even before it is spent in protest of such a bill. While we cannot control vicious legislators we can lessen the evil done by them by a campaign of education. What we cannot do singly, we can accomplish by unification, and while you or I as individuals cannot expect to influence the public mind, six hundred of us, as a unit, showing the need of sane laws and pernicious effects of vicious ones will cause somebody to take notice. Away with obsolete methods, with futile attempts to control the practice of medicine which holds us up to ridicule and are successful only in their failure. Let us have the light of publicity, refute the specious argument of the quack and combat the pernicious advertising of the nostrum vender by showing the public the absurdity of their claims, and do it openly and loudly. In a word, meet these opponents by educating the public, and when the public loses faith in quacks and quackery their field of usefulness is destroyed. This should be done with no personal animosity, no opportunity should be offered for charges of jealousy or competition, but exactly as we are trying to teach the people how to live, how to avoid tuberculosis, how their children may escape the various ills of childhood and grow to strong and healthy men and women, just so should we attempt to show how lives may be prolonged, suffering appeased and happiness secured by an escape from the thraldom of quacks and quackery.

The only hope of the future lies in education. More knowledge on health matters must mean greater efficiency, comfort and enjoyment for each individual. Public health is now recognized to be a question not of individual interest alone, but of public and collective importance. The city or the State in the future which permits its citizens of any age to sicken or die from preventable diseases will no longer be regarded as civilized. Ignorance, filth, disorder and disease must disappear as the people know and understand their causes and means of prevention. In this work the organized medical profession must assume an active part in (1) the publication of suitable material in the public press, (2) the distribution of pamphlets to the public, (3) the organization of public lecture courses, and (4) the dissemination by circular letters of matters of general moment to the medical profession.

This same spirit of prominence in everything connected with medicine if applied to the evils of hospitalism will be effectual in remedying many of its abuses. The profession should not be the servants of corporations or boards of trustees, but should be fellow workers. The conduct of great institutions should not be vested entirely with the layman and the physician be compelled to petition for relief from what seems to be an injustice.

There should be representatives from the staff on each board of trustees, either elected or selected, who should present for consideration the doctor's side of these problems and should have a voice in deciding them. Then there would be no strikes of visiting staffs, no unseemly contests or difference of opinion, no taxation service without representation. Then the profession would feel that their services, without which the hospital is impossible, were appreciated and that they were recognized as the member of a profession which had always been foremost in works of charity and chief in the desire to benefit mankind. All this may be accomplished by a unified profession, by a more thorough organization, by the elimination of personal animosities, by willing service in the fight to uphold the tenets and traditions of a glorious profession.

RHODE ISLAND AIR NATIONAL GUARD

PART TIME

MEDICAL OFFICER POSITIONS AVAILABLE

OPEN TO:
MEDICAL AND/OR
OSTEOPATHIC DOCTORS

CONTINUING MEDICAL EDUCATION

FOR MORE INFORMATION CONTACT:
COL (DR) BLAS MORENO
(401) 726-2555

"BEST PART-TIME JOB IN AMERICA"

The Doctor's Image — Past, Present, and Future

Samuel Adelson, MD

Several decades ago many homes were decorated with a picture calendar depicting "The Doctor" by Sir Luke Fildes. A little child is very ill, the bearded kind-faced doctor is sitting by her, watching her with a troubled look. The parents are seen in the background in an attitude of fear and sadness. The scene is very dramatic. Life or death is in the hands of God and the doctor. Faith in God and doctor helps the parents through their ordeal. Whatever the outcome, the doctor is still their trusted friend. They consult him on all matters — not only health. They seek his advice concerning business ventures, children's education, marriage, and all other intimate matters.

Such was the image of the family physician. He did not have to worry about a bad press, possible law suit, or third parties involved in medical care. The patient came to him when ill; he gave his best efforts, administered medicine empirically, and gave large doses of encouragement and confidence.

The image of the doctor in this day has changed but how has the doctor changed? Is the change for better or for worse? In the case of the little girl in the calendar picture who probably had pneumonia, what can the doctor do for her? His medication is practically useless, and the mortality in pneumonia may be as high as 30 per cent. The doctor of today would treat this patient in the hospital. X-rays, blood test, sputum examinations, cultures, and sensitivity tests are all available. Oxygen and specific antibiotics are available. Instead of a prolonged febrile debilitating disease, frequently the patient is practically cured in 24 hours. Neither does the doctor of today lack the kindness and concern of his predecessor. Today's doctor is steeped in scientific medicine. The drugs that he uses and the surgical procedures that he performs were unknown and not even dreamed of by the doctors of 40 years ago, 30 years ago, or even 20 years ago. He has put in many more years of study and preparation for his practice. He is not less sympathetic, but

Presidential address delivered at the Sesquicentennial Meeting of the Rhode Island Medical Society on May 9, 1962, at the Marvel Gymnasium, Brown University, Providence, Rhode Island. Reprinted from Rhode Island Medical Journal *45:297-298, June 1962.*

is accused of being impersonal and arrogant. He is blamed because he does not with to make unnecessary house calls, but he knows that the patient can derive greater benefit from an office visit or an examination at a hospital. He is accused of leaving his practice too often, but he attends many more scientific meetings and refresher courses to better enable him to treat his patients. He is blamed for the high cost of medical care, but the doctors' fees have increased much less than the cost of drugs, hospital services, and nursing care. Patients get much more for their medical fee now than ever before in terms of preventive medicine, lessened morbidity and mortality, increased longevity, decreased periods of hospitalization and convalescence, and fewer days out of work.

The doctors' image now is apparently seen through a mirror which causes a very ugly distortion. The fact is that almost every individual believes in his own doctor. He considers his doctor able, competent, honest, sympathetic. He entrusts his health and life and that of his family to the hands of his doctor and feels a sense of security. He has chosen his doctor of his own free will and discusses his medical problems with him easily and without restraint. There is a complete understanding which is mutually satisfactory and beneficial. The diagnosis is explained to the patient and also how the diagnosis is reached. The type of therapy, medical or surgical, is carefully and plainly described and all possible eventualities are explained. The patient is enlightened and the doctor does not hide behind scientific terminology and a façade of superiority. Yes, the patient likes his doctor, trusts and believes him. But the same patient is made to believe that a majority of the doctors are not like that. He is made to believe, by exaggerated newspaper stories and by irresponsible statements from people who represent selfish interests or who have political ambitions, that doctors are making too much money. That they do not deserve the fees they ask. That they abuse Physicians Service plans and other insurance companies. Unfortunately, people who make such statements are not required to substantiate their accusations by proof, and the accused is not given the opportunity to disprove these wild accusations. The newspapers are immune as long as they omit names and only print what is told to the, giving their source of misinformation. This sells newspapers and makes money. They are on firm ground legally. But, from the moral aspect, are they serving the public interest by being accessory to the act of blackening the reputation of the members of a noble profession without proof of wrong-doing? Are they carrying out the proper functions of the fourth estate? I commend the doctors of Rhode Island for maintaining their dignity under fire and for refusing to enter a name-calling contest. They feel morally strong in the knowledge that the attacks upon them are untrue and unjustified. A thousand doctors should not be subjected to abuse and suspicion for the faults of a very few.

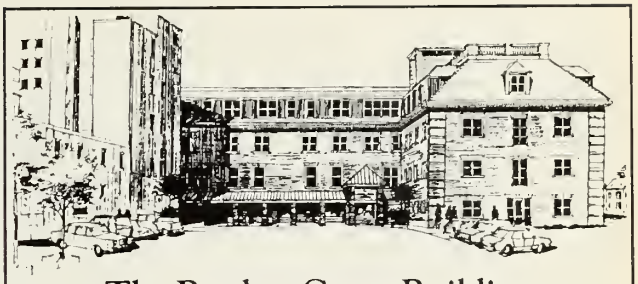
Regarding these few doctors who are proven guilty of unethical conduct, their actions cannot be condoned. Dishonesty in our profession is abhorrent and must be wiped out. Let us take an example from a universally accepted principle in treating disease. A malignant tumor must be destroyed to save the rest of the body. In a similar manner unscrupulous, dishonest doctors must be removed not only to remove suspicion from all doctors, but what is more important, to prevent them from preying on the unsuspecting public.

The American Medical Association is advocating closer contact between medical societies and state directors of professional regulation. Following this recommendation a conference was recently held by Doctor Francis Sargent, chairman of our grievance committee, and myself, with Mr. Thomas Casey, chief of the division of professional regulation, and Doctor Joseph Cannon, state director of health. It was agreed that if we find a doctor guilty of gross unprofessional conduct, in addition to the penalty imposed by the Medical Society, the matter will also be referred to the proper state agency for whatever further action is warranted. We must clean our own house of any wrongdoers, but this must be done in an orderly fashion. Charges against a doctor must be proven by evidence that will hold, and the accused must be given every opportunity to exonerate himself. There is no room in the Rhode Island Medical Society for those who abuse the public, either privately or through insurance companies, employees' compensation, or in any other way.

I believe that the distorted reflection is gradually, but definitely, being straightened out. The image of the doctor is now beginning to appear as a reasonable likeness, without wings or halo, but also without horns or cloven hoof. The campaign to lower the prestige of the individual physician and to defame the American Medical Association and state and local societies has sunk to new lows of gutter sniping. All faults or imaginary faults of the profession were grossly exag-

gerated and all great achievements were minimized or ignored. This was part of an organized plan by those who desire a total welfare state and look to the eventual socialization of medicine as well as other services. Public funds are used to further this campaign. The over 65-years-of-age men and women are transported to meeting places and told when to applaud. They are promised pie in the sky: total paternalistic care of all their needs at no cost to them. Who will pay the bill? I believe that it is immoral, improper and illegal to use public funds to further this political movement.

It appears to me that this mud-slinging has backfired. Our detractors are now seen in their true light, and their real purposes are being understood more and more. You can't fool all the people all of the time — not in America. When all the facts will be exposed to the pure light of reason and understanding, when the clouds of distrust and calumny will be dissipated, the doctor will not be found wanting; and our profession will again take its place in the minds of men of good will as a noble profession whose members are dedicated for the public good.



The Borden-Carey Building
Medical and Office Condominiums

NOW AVAILABLE FOR SALE
OR LEASE

Conveniently located at 19 Friendship St.,
Adjoining Newport Hospital

Individual Suites are now available for interior design and tenant finish.

Priced to sell from $80,000 and to lease for $15.00/s.f.

For further information call:

RE
Ryan Elliott

Ryan Elliott & Co. of Rhode Island, Inc.
401-331-0350

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

336-3600

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

MEDICAL OFFICE SPACE FOR RENT
(Furnished or Unfurnished)

Southside Medical Center
120 Dudley Street
Providence, Rhode Island

885 sq. ft.

Full or part time rental available
Next to Rhode Island Hospital
Across from Women and Infants Hospital
Full Laboratory and X-Ray Facilities

For Information Call:
Days: 331-2303
521-9290
Evenings: 885-5966

INTERNIST

PROVIDENCE

AVAILABLE IMMEDIATELY!

Community Health Center Network
seeks full-time BC/BE internist

Send CV to:

Stanley Hoyt Block, MD
Medical Director
Providence Ambulatory Health Care
Foundation, Inc.
469 Angell Street
Providence, RI 02906

or call (401) 861-6300

AN AFFIRMATIVE ACTION/EQUAL
OPPORTUNITY EMPLOYER

EMPLOYMENT OPPORTUNITIES

Family Practice Physicians
Obstetricians
Pediatricians
Internists
Dentists

are needed full and part-time for private, non-profit community health centers with expanding practices in Rhode Island.

Applicants must be board-eligible or certified. Positions are available weekdays, evenings, and Saturdays in suburban and urban centers.

Send letter of interest and curriculum vitae to:

Resources Coordinator
Rhode Island Health Center
Association
2845 Post Road, Rm. 110
Warwick, RI 02886
(401) 723-3778

NOW UNDER DEVELOPMENT
at
ASHLEY DOWNS
BIOPHARMACEUTICAL LABS

An entire new line of **NONANIMAL SOURCE** Insulins
Pūrinsulin Human® ..... nonanimal rDNA source
Pūrinsulin Pork® ..... nonanimal rDNA source
Pūrinsulin Beef® ..... nonanimal rDNA source
Pūrinsulin Beef/Pork® ..... nonanimal rDNA source

Human Tissue Plasminogen Activator (tPA)
Plasminase® ..... chemically synthesized gene product

Human Erythroprotein (EPO)
Erythröten® ..... chemically synthesized gene product

In R&D: Factor VIII; Interleukin-2; Growth Hormone

Ashley Downs Biopharmaceutical Laboratories
A NEW BIOTECH FACILITY
IN RHODE ISLAND

correspondences to:
Ashley Downs Biopharmaceutical Laboratories
909 North Main Street
Providence, RI 02904

When you want to maximize the return on your significant income and assets, call a Hospital Trust Private Banker. For maximum strategies for your financial future.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Equal Opportunity Lender

IMAGINE KNOWING THAT TODAY IS THE BEST DAY YOU'LL EVER HAVE.

If you had a progressive neuromuscular disease, every tomorrow would bring you greater weakness and more muscle waste. And the best day you could hope for would be the one you were having right now.

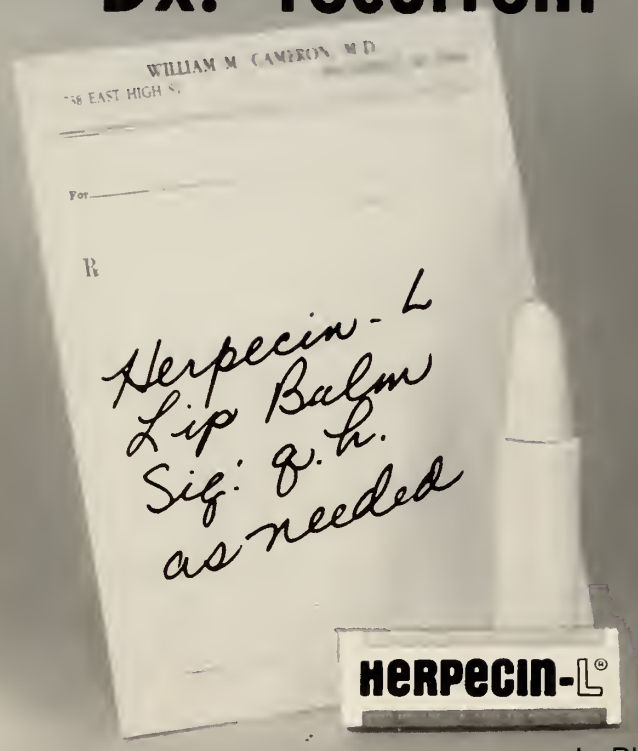
That's because most neuromuscular diseases progress day by day, gradually wasting a patient's muscles away. This muscle degeneration can't be halted. And, it can never be reversed.

At the Muscular Dystrophy Association, we're striving to put an end to twelve forms of muscular dystrophy and twenty-eight other neuromuscular diseases. Because we believe there are no incurable diseases—just diseases for which cures haven't yet been found. And because it's the only way that tens of thousands of people with neuromuscular disease can look forward to a better tomorrow.

MDA

Muscular Dystrophy Association, Jerry Lewis, National Chairman

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms . . .** blisters **never formed . . .** remarkable." DH, MA

"(In clinical trials) **. . . response** was **dramatic. HERPECIN-L . .** proven **far superior.**" DDS, PA

"All patients claimed **shorter duration . . .** at **prodromal symptoms . . .** HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: **CAMPBELL LABORATORIES, INC.,** P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

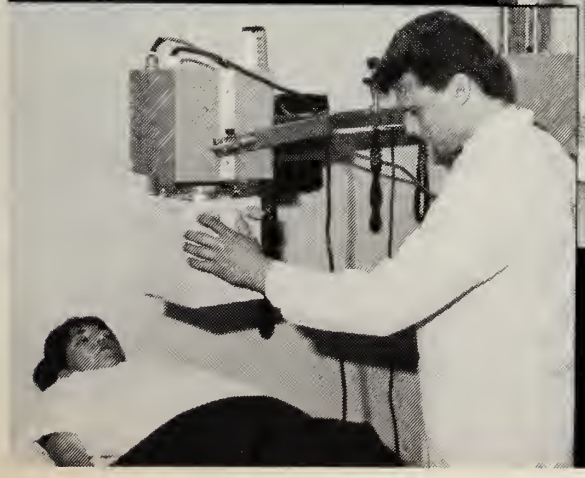
We've become the largest full service medical lab in Rhode Island... *because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

CARAFATE®
(sucralfate)

BRIEF SUMMARY

CONTRAINDICATIONS
There are no known contraindications to the use of sucralfate.

PRECAUTIONS
Duodenal ulcer is a chronic, recurrent disease. While short-term treatment with sucralfate can result in complete healing of the ulcer, a successful course of treatment with sucralfate should not be expected to alter the post-healing frequency or severity of duodenal ulceration.

Drug Interactions: Animal studies have shown that the simultaneous administration of CARAFATE with tetracycline, phenytoin, or cimetidine will result in a statistically significant reduction in the bioavailability of these agents. This interaction appears to be nonsystemic in origin, presumably resulting from these agents being bound by CARAFATE in the gastrointestinal tract. The bioavailability of these agents may be restored simply by separating the administration of these agents from that of CARAFATE by two hours. The clinical significance of these animal studies is yet to be defined.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No evidence of drug-related tumorigenicity was found in chronic oral toxicity studies of 24 months' duration conducted in mice and rats at doses up to 1 gm/kg (12 times the human dose). A reproduction study in rats at doses up to 38 times the human dose did not reveal any indication of fertility impairment. Mutagenicity studies have not been conducted.

Pregnancy: Pregnancy Category B. Teratogenicity studies have been performed in mice, rats, and rabbits at doses up to 50 times the human dose and have revealed no evidence of harm to the fetus due to sucralfate. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when sucralfate is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Adverse reactions to sucralfate in clinical trials were minor and only rarely led to discontinuation of the drug. In studies involving over 2,500 patients, adverse effects were reported in 121 (4.7%). Constipation was the most frequent complaint (2.2%). Other adverse effects, reported in no more than one of every 350 patients, were diarrhea, nausea, gastric discomfort, indigestion, dry mouth, rash, pruritus, back pain, dizziness, sleepiness, and vertigo.

DOSAGE AND ADMINISTRATION
The recommended adult oral dosage for duodenal ulcer is 1 gm four times a day on an empty stomach.

Antacids may be prescribed as needed for relief of pain but should not be taken within one-half hour before or after sucralfate.

While healing with sucralfate may occur during the first week or two, treatment should be continued for 4 to 8 weeks unless healing has been demonstrated by x-ray or endoscopic examination.

HOW SUPPLIED
CARAFATE (sucralfate) 1-gm pink tablets are supplied in bottles of 100 and in Unit Dose Identification Paks of 100. The tablets are embossed with MARION/1712. Issued 3/84

References:

1. Korman MG, Shaw RG, Hansky J, et al: *Gastroenterology* 80:1451-1453, 1981.
2. Korman MG, Hansky J, Merrett AC, et al: *Dig Dis Sci* 27:712-715, 1982.
3. Brandstaetter G, Kratochvil P: *Am J Med* 79(suppl 2C):36-38, 1985.
4. Marks IN, Wright JP, Gilinsky NH, et al: *J Clin Gastroenterol* 8:419-423, 1986.
5. Lam SK, Hui WM, Lau WY, et al: *Gastroenterology* 92:1193-1201, 1987.

Another patient benefit product from
PHARMACEUTICAL DIVISION
MARION LABORATORIES INC.
KANSAS CITY MO 64137

1594H7

Ulcer therapy that won't yield, even to smoking

What do you do for duodenal ulcer patients who should stop smoking, but won't? Both cimetidine[1] and ranitidine[2] have been shown less effective in smokers than nonsmokers.

Choose CARAFATE® (sucralfate/Marion). Two recent studies show Carafate to be as effective in smokers as nonsmokers.[3,4] A difference further illustrated in a 283-patient study comparing sucralfate to cimetidine[5]:

Ulcer healing rates:
(at four weeks of therapy)[5]

Sucralfate:	
All patients	79.4%
Smokers	81.6%*
Cimetidine:	
All patients	76.3%
Smokers	62.5%

*Significantly greater than cimetidine smoker group ($P<.05$).

Carafate has a unique, nonsystemic mode of action that enhances the body's own ulcer healing ability and protects the damaged mucosa from further injury.

When your ulcer patient is a smoker, prescribe the ulcer medication that won't go up in smoke: safe, nonsystemic Carafate.

Nothing works like

CARAFATE®
sucralfate/Marion

Please see adjoining page for references and brief summary of prescribing information.

1594H7

There's never been a better time for her...

and PREMARIN®

Proven benefits beyond relief of vasomotor symptoms

No other estrogen proven effective for osteoporosis

Only conjugated estrogens tablets have established efficacy in both osteoporosis[1] and vasomotor symptoms* at 0.625 mg/day. No other estrogen, oral or transdermal, has established clinical evidence or minimum effective dose in both indications.

No estrogen proven safer

PREMARIN is the most extensively tested estrogen, with an unsurpassed record of long-term safety.
And clinical evidence shows a significantly reduced risk of endometrial hyperplasia when cycled with a progestin.[2]

PREMARIN®
(conjugated estrogens tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms and for osteoporosis

PREMARIN®
(conjugated estrogens tablets)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(conjugated estrogens)

Vaginal Cream

0.625 mg/g

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS.)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream, in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA

Three independent, case-controlled studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case-controlled studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semi-annual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equi-estrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a nonsteroidal estrogen, have an increased risk of developing, in later life, a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb-reduction defects. One case-controlled study estimated a 4.7-fold increased risk of limb-reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb-reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well-controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP): Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) Osteoporosis (abnormally low bone mass). Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae.

PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (see Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Estrogens have been reported to increase the risk of endometrial carcinoma (see Boxed Warning). However, a recent large, case-controlled study indicated no increase in risk of breast cancer in postmenopausal women. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism, and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention, such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Pre-existing uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not yet complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T_3 by column, or T_4 by radioimmunoassay. Free T_3 resin uptake is decreased, reflecting the elevated TBG; free T_4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration.

As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

Long-term, continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. However, in a recent, large case-controlled study of postmenopausal women there was no increase in risk of breast cancer with use of conjugated estrogens.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow, dysmenorrhea, premenstrual-like syndrome, amenorrhea during and after treatment, increase in size of uterine fibromyomata, vaginal candidiasis, change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome, tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating, cholestatic jaundice, chloasma or melasma which may persist when drug is discontinued, erythema multiforme, erythema nodosum, hemorrhagic eruption, loss of scalp hair, hirsutism, steepening of corneal curvature, intolerance to contact lenses, headache, migraine, dizziness, mental depression, chorea, increase or decrease in weight, reduced carbohydrate tolerance, aggravation of porphyria, edema, changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only:* For treatment of moderate-to-severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 mg to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically:* Osteoporosis. Female castration. Osteoporosis—0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off). Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control.

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only: For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three- to six-month intervals.

Usual dosage range: 2 g to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Lindsay R, Hart DM, Clark DM: The minimum effective dose of estrogen for prevention of postmenopausal bone loss. *Obstet Gynecol* 1984;63:759-763. **2.** Studd JWW, Thom MH, Paterson MEL, et al: The prevention and treatment of endometrial pathology in postmenopausal women receiving exogenous estrogens, in Pasetto N, Paoletti R, Ambrus JL (eds): *The Menopause and Postmenopause*. Lancaster, England, MTP Press Ltd, 1980, chap 13.

© 1987 Ayerst Laboratories
All rights reserved

6437/587

Ayerst. AYERST LABORATORIES
New York, NY 10017

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...

...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol — which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were treated merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA

The one you know best keeps looking better

NOW AVAILABLE...
NEW LOW DOSE
INDERAL LA 60 mg
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)*

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. INDERAL LA is formulated to provide a sustained release of propranolol hydrochloride. INDERAL LA is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective beta-adrenergic receptor blocking agent, possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (60, 80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period, the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL Tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg-for-mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

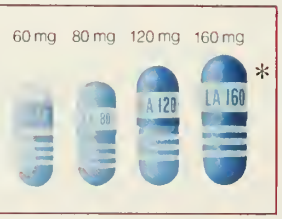
Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in: 1) cardiogenic shock, 2) sinus bradycardia and greater than first-degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl)
LONG ACTING CAPSULES



WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (eg, chronic bronchitis, emphysema) PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta blockers should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. Following insulin-induced hypoglycemia, propranolol may cause a delay in the recovery of blood glucose to normal levels.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol may change thyroid function tests, increasing T_4 and reverse T_3, and decreasing T_3.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. GENERAL. Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

CLINICAL LABORATORY TESTS. Elevated blood urea levels in patients with severe heart disease; elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Caution should be exercised when patients receiving a beta blocker are administered a calcium-channel blocking drug, especially intravenous verapamil, for both agents may depress myocardial contractility or atrioventricular conduction. On rare occasions, the concomitant intravenous use of a beta blocker and verapamil has resulted in serious adverse reactions especially in patients with severe cardiomyopathy, congestive heart failure or recent myocardial infarction.

Aluminum hydroxide gel greatly reduces intestinal absorption of propranolol.

Ethanol slows the rate of absorption of propranolol.

Phenytoin, phenobarbitone, and *rifampin* accelerate propranolol clearance.

Chlorpromazine, when used concomitantly with propranolol, results in increased plasma levels of both drugs.

Antipyrine and *lidocaine* have reduced clearance when used concomitantly with propranolol.

Thyroxine may result in a lower than expected T_3 concentration when used concomitantly with propranolol.

Cimetidine decreases the hepatic metabolism of propranolol, delaying elimination and increasing blood levels.

Theophylline clearance is reduced when used concomitantly with propranolol.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

PREGNANCY. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose. There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS. INDERAL is excreted in human milk. Caution should be exercised when INDERAL (propranolol HCl) is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. Bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System. Light-headedness; mental depression manifested by insomnia; lassitude; weakness; fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; vivid dreams; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss; emotional lability; slightly clouded sensorium; and decreased performance on neuropsychometrics. For immediate formulations, fatigue, lethargy, and vivid dreams appear dose related.

Gastrointestinal. Nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. Pharyngitis and agranulocytosis; erythematous rash; fever combined with aching and sore throat; laryngospasm and respiratory distress.

Respiratory. Bronchospasm.

Hematologic. Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. Alopecia; LE-like reactions; psoriasiform rashes; dry eyes; male impotence; and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL Tablets to INDERAL LA Capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg-for-mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION—*Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS—*Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three- to seven-day intervals until optimal response is obtained. Although individual patients may respond at any dosage level, the average optimal dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE—*Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimal migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximal dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS—80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE—At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985; 145:1321-1323.

1R7119/887

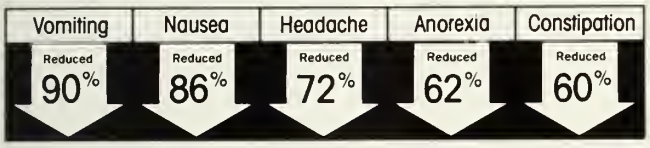
Ayerst AYERST LABORATORIES
New York, NY 10017

© 1987 Ayerst Laboratories

See the difference in the first week[1]

- **Sleep improvement in 74% of patients after first h.s. dose[2]**
- **Significantly faster relief–62% of total four-week improvement evident in first week versus 44% with amitriptyline alone[1]**
- **Dramatic first-week reduction in somatic complaints[2]**

% Reduction in Somatic Symptoms[2]



- **Only ⅓ the dropout rate due to side effects of amitriptyline alone, although the incidence of side effects is similar[1]**

Caution patients about the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to the lowest effective amount in elderly patients.

Protect your decision.
Write "Do not substitute."

In moderate depression and anxiety

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) (IV)

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) (IV)

Copyright © 1987 by Roche Products Inc. All rights reserved.

References: 1. Feighner JP, *et al: Psychopharmacology 61*:217-225, Mar 22, 1979 **2.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ

Limbitrol® (IV)
Tranquilizer—Antidepressant
Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of moderate to severe depression associated with moderate to severe anxiety
Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use, then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.
Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

***Usage in Pregnancy*: Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage. Withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).
Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.
Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.
The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs.
Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.
Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.
Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.
Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.
Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.
Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.
Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.
Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.
Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.
Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. IV administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.
Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly. Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.
How Supplied: *Double strength (DS) Tablets*, white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets*, blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500, Tel-E-Dose® packages of 100, Prescription Paks of 50.

ROCHE®
ROCHE PRODUCTS INC
Manati, Puerto Rico 00701

PI 0585

The rewards of Limbitro
You're both smiling agai

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

See the difference in the first week[1]

In depressed and anxious patients, you can see the difference sooner—62% of total four-week improvement achieved in the first week with Limbitrol versus 44% with amitriptyline.[1]

In moderate depression and anxiety

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓒ Ⓒ Ⓒ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓒ Ⓒ Ⓒ

ROCHE®

Please see summary of product information on adjacent page.

Rhode Island Medical Journal

October 1987
Volume 70, Number 10

DISPLAY SHELVES

Doctor Elisha Bartlett, distinguished medical educator, writer, and philosopher
(See page 449)

CONTRIBUTIONS

435 **Cancer Control in Rhode Island: Part 1. The Value of Screening for Cancer**

441 **Acquired Immune Deficiency Syndrome (AIDS) and the Obstetrical Team**

449 **A Rhode Island Philosopher (Elisha Bartlett)**

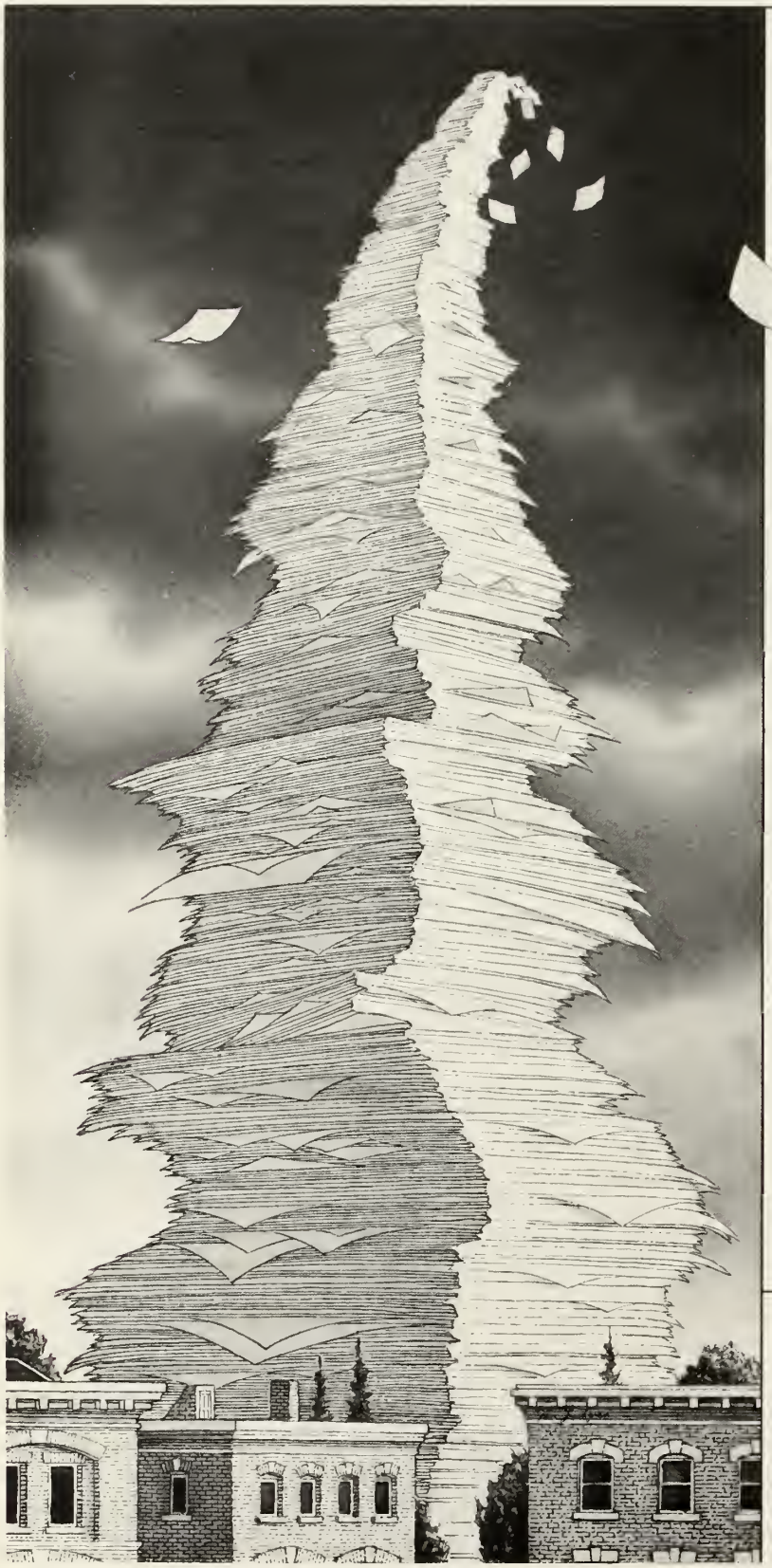
443 **EDITORIAL**

464 **INFORMATION FOR AUTHORS**

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

OCT 28 1987

FINANCE YOUR INVESTMENTS WITHOUT INVESTING A LOT OF YOUR TIME.



When you've set your sights on a new medical office, computer system, or piece of real estate, your Private Banker at Bank of New England-Old Colony can make financing your investment as easy for you as writing a prescription.

No one understands your specialized needs and professional situation—and the way through the maze of tax laws, loan procedures, and red tape attendant with meeting your financing objectives—better than your Private Banker. Once your plan is in motion, this special banking relationship will continue to work to your benefit with ongoing timely and accurate financial counseling and direction. And our expert assistance is available to you without additional fees or extra charges of any kind.

With a responsive expert handling every detail of your financial requirements, you can continue doing what you do best without missing a beat.

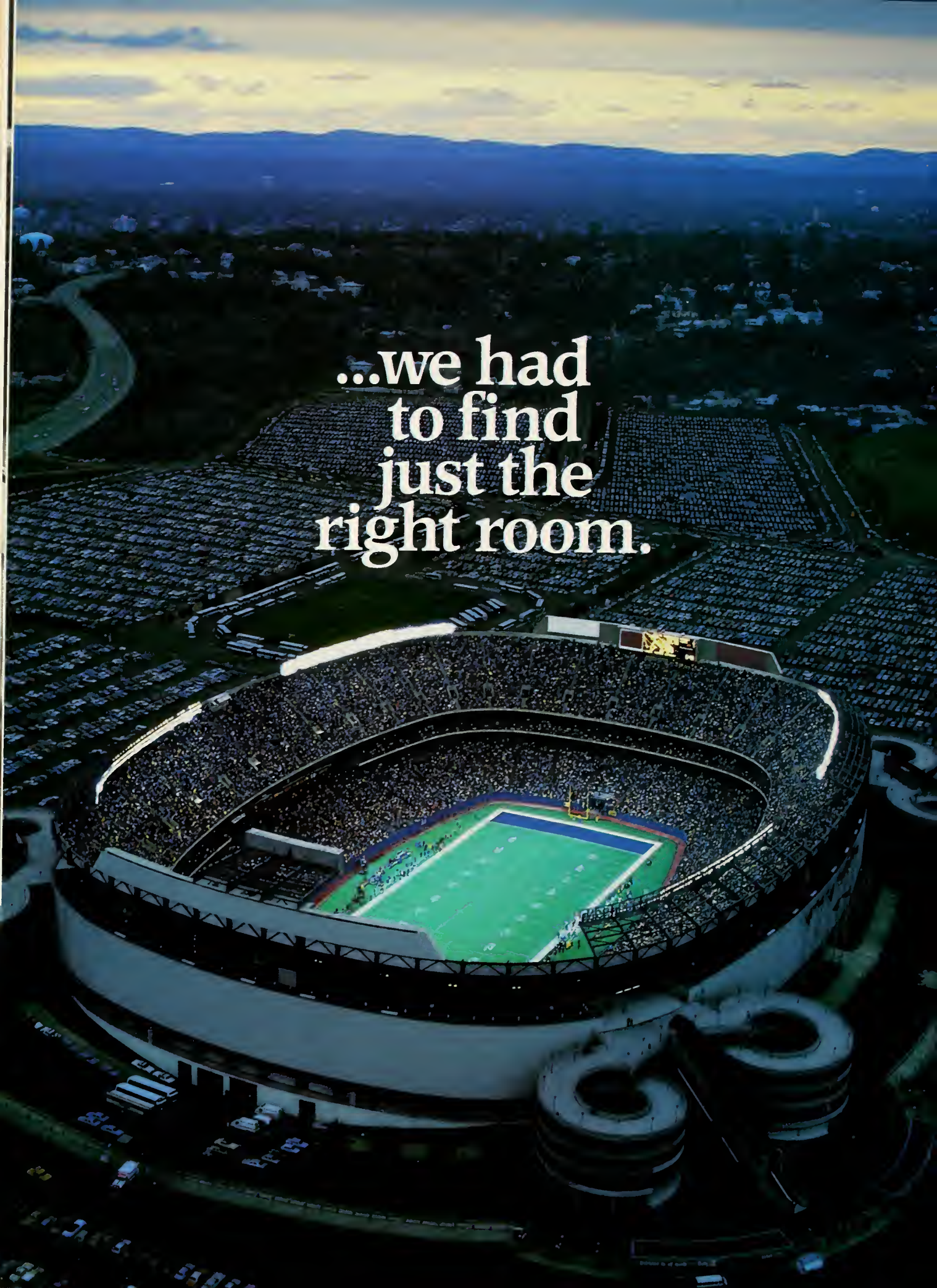
Call Dick Boenning, Director of Private Banking, at 575-2050.

PRIVATE BANKING

BANK OF NEW ENGLAND
OLD COLONY

We take your financial goals personally.
Member FDIC

To show you how many hypertensives stayed on INDERAL® LA (PROPRANOLOL HCl) after a major nationwide trial...


...we had
to find
just the
right room.

60,073 patients (90%) who started on INDERAL LA stayed on INDERAL LA.[1*]

Surprising? Not really.

Because most patients on INDERAL LA (propranolol HCl) don't even know it's working.
A recent double-blind, placebo-controlled, crossover study in 138 hypertensive patients[2] revealed that INDERAL LA has a side effects profile unsurpassed by atenolol or metoprolol—which shows how well-tolerated once-daily INDERAL LA can be.

Sole therapy or concomitant therapy? Fifty-nine percent of the time, INDERAL LA stood on its own.

The patients in the nationwide compliance trial were no different from yours. Generally when the antihypertensive regimen is complicated, compliance may become a problem. So, the effectiveness of INDERAL LA as once-daily monotherapy is a big plus. Of the remaining hypertensives in the program, 36% were treated merely with the addition of a diuretic to INDERAL LA.

For the noncompliant patients in your practice, INDERAL LA may well be the answer.

Almost 20,000 of the patients in the nationwide compliance trial were identified as having been noncompliant with their previous antihypertensive therapy. Their physicians reported that 88% showed improved compliance when placed on once-daily INDERAL LA.

Control, comfort, and compliance

ONCE-DAILY
INDERAL® LA
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Like conventional INDERAL Tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, cardiogenic shock, heart block greater than first degree, and bronchial asthma.

*After a 30-day trial with INDERAL LA, physicians reported that 90% of the patients would remain on INDERAL LA

The one you know best keeps looking better

NOW AVAILABLE...
NEW LOW DOSE
INDERAL LA 60 mg
(PROPRANOLOL HCl) LONG ACTING CAPSULES

Please see next page for brief summary of prescribing information

The one you know best keeps looking better

BRIEF SUMMARY (*FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.*)

INDERAL® LA brand of propranolol hydrochloride **(Long Acting Capsules)**

DESCRIPTION. INDERAL LA is formulated to provide a sustained release of propranolol hydrochloride. INDERAL LA is available as 60 mg, 80 mg, 120 mg, and 160 mg capsules.

CLINICAL PHARMACOLOGY. INDERAL is a nonselective, beta-adrenergic receptor-blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. When access to beta-receptor sites is blocked by INDERAL, the chronotropic, inotropic, and vasodilator responses to beta-adrenergic stimulation are decreased proportionately.

INDERAL LA Capsules (60, 80, 120, and 160 mg) release propranolol HCl at a controlled and predictable rate. Peak blood levels following dosing with INDERAL LA occur at about 6 hours and the apparent plasma half-life is about 10 hours. When measured at steady state over a 24-hour period, the areas under the propranolol plasma concentration-time curve (AUCs) for the capsules are approximately 60% to 65% of the AUCs for a comparable divided daily dose of INDERAL Tablets. The lower AUCs for the capsules are due to greater hepatic metabolism of propranolol, resulting from the slower rate of absorption of propranolol. Over a twenty-four (24) hour period, blood levels are fairly constant for about twelve (12) hours then decline exponentially.

INDERAL LA should not be considered a simple mg-for-mg substitute for conventional propranolol and the blood levels achieved do not match (are lower than) those of two to four times daily dosing with the same dose. When changing to INDERAL LA from conventional propranolol, a possible need for retitration upwards should be considered, especially to maintain effectiveness at the end of the dosing interval. In most clinical settings, however, such as hypertension or angina where there is little correlation between plasma levels and clinical effect, INDERAL LA has been therapeutically equivalent to the same mg dose of conventional INDERAL as assessed by 24-hour effects on blood pressure and on 24-hour exercise responses of heart rate, systolic pressure and rate pressure product. INDERAL LA can provide effective beta blockade for a 24-hour period.

INDICATIONS AND USAGE. Hypertension: INDERAL LA is indicated in the management of hypertension; it may be used alone or used in combination with other antihypertensive agents, particularly a thiazide diuretic. INDERAL LA is not indicated in the management of hypertensive emergencies.

Angina Pectoris Due to Coronary Atherosclerosis: INDERAL LA is indicated for the long-term management of patients with angina pectoris.

Migraine: INDERAL LA is indicated for the prophylaxis of common migraine headache. The efficacy of propranolol in the treatment of a migraine attack that has started has not been established and propranolol is not indicated for such use.

Hypertrophic Subaortic Stenosis: INDERAL LA is useful in the management of hypertrophic subaortic stenosis, especially for treatment of exertional or other stress-induced angina, palpitations, and syncope. INDERAL LA also improves exercise performance. The effectiveness of propranolol hydrochloride in this disease appears to be due to a reduction of the elevated outflow pressure gradient which is exacerbated by beta-receptor stimulation. Clinical improvement may be temporary.

CONTRAINDICATIONS. INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first-degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

ONCE-DAILY

INDERAL® LA

(PROPRANOLOL HCl)

LONG ACTING CAPSULES

60 mg 80 mg 120 mg 160 mg

*

WARNINGS. CARDIAC FAILURE. Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary, they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely; or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following *abrupt* discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned, the dosage should be gradually reduced over at least a few weeks, and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (eg, chronic bronchitis, emphysema) — PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY. The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL (propranolol HCl), like other beta-blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, eg, dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA. Beta blockers should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. Following insulin-induced hypoglycemia, propranolol may cause a delay in the recovery of blood glucose to normal levels.

THYROTOXICOSIS. Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol may change thyroid function tests, increasing T_4 and reverse T_3, and decreasing T_3.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case, this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS. GENERAL. Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL (propranolol HCl) is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

CLINICAL LABORATORY TESTS. Elevated blood urea levels in patients with severe heart disease; elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS. Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Caution should be exercised when patients receiving a beta blocker are administered a calcium-channel-blocking drug, especially intravenous verapamil, for both agents may depress myocardial contractility or atrioventricular conduction. On rare occasions, the concomitant intravenous use of a beta blocker and verapamil has resulted in serious adverse reactions especially in patients with severe cardiomyopathy, congestive heart failure or recent myocardial infarction.

Aluminum hydroxide gel greatly reduces intestinal absorption of propranolol.

Ethanol slows the rate of absorption of propranolol.

Phenytoin, phenobarbitone, and *rifampin* accelerate propranolol clearance.

Chlorpromazine, when used concomitantly with propranolol, results in increased plasma levels of both drugs.

Antipyrine and *lidocaine* have reduced clearance when used concomitantly with propranolol.

Thyroxine may result in a lower than expected T_3 concentration when used concomitantly with propranolol.

Cimetidine decreases the hepatic metabolism of propranolol, delaying elimination and increasing blood levels.

Theophylline clearance is reduced when used concomitantly with propranolol.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY. Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

PREGNANCY. Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose. There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS. INDERAL is excreted in human milk. Caution should be exercised when INDERAL (propranolol HCl) is administered to a nursing woman.

PEDIATRIC USE. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS. Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular. Bradycardia, congestive heart failure, intensification of AV block, hypotension, paresthesia of hands, thrombocytopenic purpura, arterial insufficiency, usually of the Raynaud type.

Central Nervous System. Light-headedness, mental depression manifested by insomnia, lassitude, weakness, fatigue, reversible mental depression progressing to catatonia, visual disturbances, hallucinations, vivid dreams, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics. For immediate formulations, fatigue, lethargy and vivid dreams appear dose related.

Gastrointestinal. Nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic. Pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory. Bronchospasm.

Hematologic. Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune. In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous. Alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

DOSAGE AND ADMINISTRATION. INDERAL LA provides propranolol hydrochloride in a sustained-release capsule for administration once daily. If patients are switched from INDERAL Tablets to INDERAL LA Capsules, care should be taken to assure that the desired therapeutic effect is maintained. INDERAL LA should not be considered a simple mg-for-mg substitute for INDERAL. INDERAL LA has different kinetics and produces lower blood levels. Retitration may be necessary, especially to maintain effectiveness at the end of the 24-hour dosing interval.

HYPERTENSION — *Dosage must be individualized.* The usual initial dosage is 80 mg INDERAL LA once daily, whether used alone or added to a diuretic. The dosage may be increased to 120 mg once daily or higher until adequate blood-pressure control is achieved. The usual maintenance dosage is 120 to 160 mg once daily. In some instances a dosage of 640 mg may be required. The time needed for full hypertensive response to a given dosage is variable and may range from a few days to several weeks.

ANGINA PECTORIS — *Dosage must be individualized.* Starting with 80 mg INDERAL LA once daily, dosage should be gradually increased at three- to seven-day intervals until optimal response is obtained. Although individual patients may respond at any dosage level, the average optimal dosage appears to be 160 mg once daily. In angina pectoris, the value and safety of dosage exceeding 320 mg per day have not been established.

If treatment is to be discontinued, reduce dosage gradually over a period of a few weeks (see WARNINGS).

MIGRAINE — *Dosage must be individualized.* The initial oral dose is 80 mg INDERAL LA once daily. The usual effective dose range is 160-240 mg once daily. The dosage may be increased gradually to achieve optimal migraine prophylaxis. If a satisfactory response is not obtained within four to six weeks after reaching the maximal dose, INDERAL LA therapy should be discontinued. It may be advisable to withdraw the drug gradually over a period of several weeks.

HYPERTROPHIC SUBAORTIC STENOSIS — 80-160 mg INDERAL LA once daily.

PEDIATRIC DOSAGE — At this time the data on the use of the drug in this age group are too limited to permit adequate directions for use.

*The appearance of these capsules is a registered trademark of Ayerst Laboratories.

REFERENCES:

1. INDERAL LA National Compliance Evaluation Program. Data on file, Ayerst Laboratories.
2. Ravid M, Lang R, Jutrin I. The relative antihypertensive potency of propranolol, oxprenolol, atenolol, and metoprolol given once daily. *Arch Intern Med* 1985; 145:1321-1323.

1R7119/887

Ayerst AYERST LABORATORIES
New York, NY 10017

© 1987 Ayerst Laboratories

Rhode Island Medical Journal

October 1987
Volume 70, Number 10

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Edward R. Feller, MD
Chairman

*Stanley M. Aronson, MD
Contributing Editor

*Maurice M. Albala, MD

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

*John F. W. Gilman, MD

*Edwin J. Henrie, MD

*Toussaint A. Leclercq, MD

Robert V. Lewis, MD

Robert Powel
Student

*Peter L. Mathieu, Jr., MD

*P. Joseph Pesare, MD

*Sumner Raphael, MD

Henry T. Randall, MD

*Guy A. Settipane, MD

*David T. Barrall, MD
Resident

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

OCT 28 1987

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

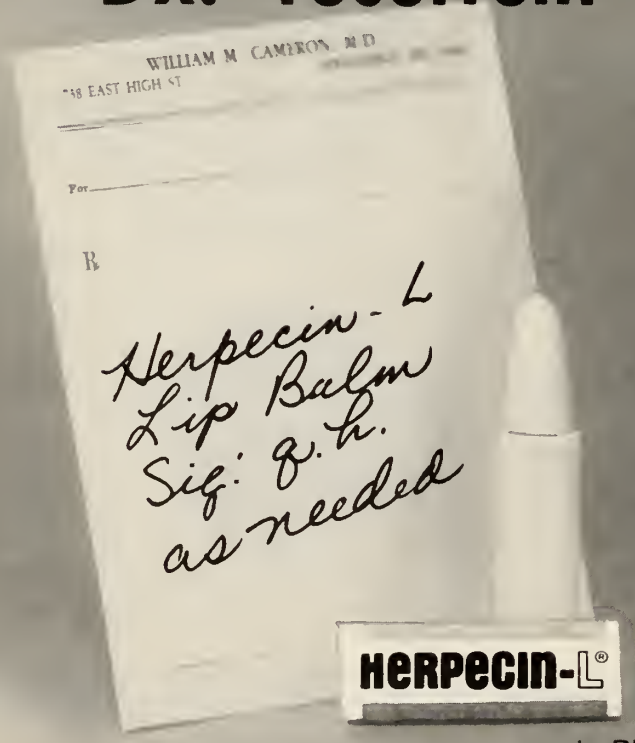
COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

1-800-521-7974

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

Volume 70, Number 10 October 1987

TABLE OF CONTENTS

433 **EDITORIAL**

A New Tool for Cancer Detection?

Seebert J. Goldowsky, MD

CONTRIBUTIONS

435 **Cancer Control in Rhode Island: Part 1. The Value of Screening for Cancer**

More Intense Cancer Screening and Education will Reduce Cancer Mortality and Morbidity in the State

Julie G. Beitz, MD
Alan B. Weitberg, MD

441 **Acquired Immune Deficiency Syndrome (AIDS) and the Obstetrical Team**

Strict Precautions Are Essential For All Exposed Personnel

Yusef Barcohana, MD

449 **A Rhode Island Philosopher (Elisha Bartlett)**

The Annual Address Delivered December 7, 1899

William Osler, MD

COVER: *Photograph of Doctor Elisha Bartlett (1803-1855), Smithfield, RI native and honorary member of the Rhode Island Medical Society.*

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue	120 Dudley Street	154 Waterman Street	38 Hamlet Avenue
Providence, R.I.	Providence, R.I.	Providence, R.I.	Woonsocket, R.I.
331-3996	331-3996	273-0450	766-4224

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℞

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

PSYCHIATRIST

The New Bedford Area Center for Human Services, Inc.

is recruiting for full and part-time positions. We are a large, out-patient community mental health center in Southeastern Mass. This is an opportunity to work in multidisciplinary programs for adult, child, aftercare, alcohol and drug treatment.
Excellent salary.

Send C.V. to:

Executive Director
New Bedford Area Center for Human Services, Inc.
P.O. Box A-2097
New Bedford, MA 02741
EOE
(617)999-2321

BLACK HORSE FARM

EXETER, RI

Exceptional
Country Homesites
of 4 Acres

$79,900

(401) 739-1135
(617) 362-2561

INTERNIST

PROVIDENCE

AVAILABLE IMMEDIATELY!

Community Health Center Network seeks full-time BC/BE internist

Send CV to:

Stanley Hoyt Block, MD
Medical Director
Providence Ambulatory Health Care Foundation, Inc.
469 Angell Street
Providence, RI 02906

or call (401) 861-6300

AN AFFIRMATIVE ACTION/EQUAL OPPORTUNITY EMPLOYER

NOW UNDER DEVELOPMENT
at
ASHLEY DOWNS
BIOPHARMACEUTICAL LABS

An entire new line of **NONANIMAL SOURCE** Insulins
Pūrinsulin Human® ..... nonanimal rDNA source
Pūrinsulin Pork® ..... nonanimal rDNA source
Pūrinsulin Beef® ..... nonanimal rDNA source
Pūrinsulin Beef/Pork® ..... nonanimal rDNA source

Human Tissue Plasminogen Activator (tPA)
Plasminase® ..... chemically synthesized gene product

Human Erythroprotein (EPO)
Erythrōten® ..... chemically synthesized gene product

In R&D: Factor VIII; Interleukin-2; Growth Hormone

Ashley Downs Biopharmaceutical Laboratories
A NEW BIOTECH FACILITY
IN RHODE ISLAND

correspondences to:
Ashley Downs Biopharmaceutical Laboratories
909 North Main Street
Providence, RI 02904

EDITORIAL

A New Tool for Cancer Detection?

Nuclear magnetic resonance (NMR) as an imaging technique in clinical medicine is of fairly recent origin, but as nuclear resonance spectroscopy in chemical analysis it has been around for more than two decades. Doctor Eric Fossel, a PhD radiologist at the Beth Israel Hospital in Boston and at Harvard Medical School, with a strong background in organic chemistry, has taken advantage of a new development designated as water suppressed photon nuclear resonance spectroscopy to apply NMR spectroscopy to blood analysis.

NMR spectra reveal the presence of hydrogen atoms in molecules and in media bearing the molecules. Thus, NMR spectra of biological samples containing varying amounts of water, which is of course H_2O, are dominated by a large water peak. Blood, which is mostly water, displays such a peak. The advent of water suppression has circumvented this difficulty. The presence of hydrogen peaks for the lipid chains of lipoproteins with their high hydrogen content was obscured in blood samples by the high water content of blood. Water suppression permits the peaks for the lipids of plasma lipoproteins to stand out from other signals. The width of the peaks for lipoproteins is revealing of the presence or absence of cancer. Values for the average line width were lower in patients with cancer.

Doctor Fossel was supplied with ten blood samples by Doctor Jan McDonagh, pathologist of Beth Israel Hospital, and his wife. Five samples were from cancer patients and five from healthy controls. Doctor Fossel was able readily to distinguish between the samples. The peak widths were obviously and measurably narrower in patients with malignant disease than in the healthy controls. He then examined blood samples from more than three hundred (331) patients, some with a variety of malignant lesions (both solid tumors and dispersed cancers), some with benign tumors or nonmalignant disorders, and finally a sampling of healthy individuals. The previous results were clearly confirmed. The work is continuing.

For the present Doctor Fossel feels that this is a research rather than a diagnostic procedure. However, he reports that it has been quite accurate in monitoring treatment and remissions. It may prove to be useful as the first step in a diagnostic algorithm where a patient complains of feeling unwell and routine tests are negative, thus initially deferring more invasive procedures. Doctor Fossel does not deem the test to be ready for mass screening for cancer of normal subjects at this stage of development. Large prospective clinical trials will be necessary to determine the value of the test for screening of populations. Application in the clinical setting must also await additional clinical trials. Water suppressed proton NMR spectroscopy, however, appears to be a very promising development.

Seebert J. Goldowsky, MD

References

[1] Fossel, ET; Carr, JM; and McDonagh, J: Detection of Malignant Tumors. Water-Suppressed Protein Nuclear Resonance Spectroscopy of Plasma. N Engl J Med 315:1369-76, 1986.

[2] Harvard Magazine V. 90, no. 1, Sept-Oct 1987, pp 4 and 6.

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml *(1 teaspoonful)* contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg *(warning: may be habit forming)*; alcohol, 3.5 percent; in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

Cancer Control in Rhode Island: Part 1. The Value of Screening for Cancer

More Intense Cancer Screening and Education will Reduce Cancer Mortality and Morbidity in the State

Julie G. Beitz, MD
Alan B. Weitberg, MD

Introduction

The term screening for cancer refers to the application of examinations or tests to detect cancer in otherwise asymptomatic individuals. The screening process usually does not yield a definitive diagnosis. It may exclude the likelihood of cancer or identify abnormalities that require additional investigation.

Julie G. Beitz, MD is Assistant Professor of Medicine, Brown University, and Staff Physician, Division of Hematology/Oncology, Roger Williams Cancer Center, Providence, Rhode Island.

Alan B. Weitberg, MD is Assistant Professor of Medicine, Brown University, and Chief, Division of Hematology/Oncology, Roger Williams Cancer Center, Providence, Rhode Island.

Division of Hematology/Oncology, Roger Williams Cancer Center and the Department of Medicine, Brown University, Providence, Rhode Island

The rationale for screening for breast, colorectal, or cervical cancer is detection and treatment of disease at an early stage prior to the development of metastases, in order to reduce mortality. For certain other cancer sites, however, screening has not appreciably lowered mortality. This is particularly true for lung cancer. Thus, cancer control efforts related to lung cancer have focused instead on prevention of the disease, that is, on reduction of smoking incidence.

The National Cancer Institute (NCI) has set as its goal a 50 per cent reduction in the age-adjusted cancer mortality rate by the year 2000. In this paper we shall discuss the potential of cancer screening in the detection of early cancer and the reduction of mortality in breast, cervical, and colorectal cancer. In the second part of this series, we shall describe in detail the Roger Williams Cancer Screening Program, which has incorporated comprehensive cancer screening and public education activities into a hospital-based program. Finally, we shall suggest how we may improve and accelerate cancer screening activities in Rhode Island, so that we may achieve national goals.

The Problem: Rising Cancer Incidence and Mortality

Cancer mortality rates in the Northeast region of the United States have generally been among the highest in the country. For the last two years, Rhode Island has had the highest cancer mortality rate in the United States, 263/100,000 population.[1] Several factors potentially contribute to the high cancer incidence and mortality in Rhode Island. The state is highly industrialized, is densely populated especially in urban areas, and has a large elderly population.

The three anatomic sites that account for one half of new cancer cases and cancer deaths in Rhode Island are lung, colorectal, and breast cancer. Of particular concern is colorectal cancer: Rhode Island has one of the highest incidence and mortality rates in the country for this disease. Moreover, the divergence between the Rhode Island and the United States mortality rates for colorectal cancer is increasing. The following estimates are based on data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program (1981-1983) and from the Rhode Island Cancer Information System (CIS) which registered cancer cases statewide from 1978-1980.[1,2]

It is estimated that in 1987 some 650 Rhode Island women will develop breast cancer, of whom 250 will die of the disease. Ninety per cent of breast cancers will arise in women over 45 years of age. In over half of the cases, the cancer will have metastasized to regional or distant sites by the time of diagnosis. The vast majority, over 90 per cent, will undergo surgery plus additional therapy with radiation, cytotoxic agents or hormones.

It is further estimated that there will be 950 new cases of colorectal cancer and 700 new cases of lung cancer in Rhode Island in 1987. These two cancer sites together will result in approximately 1000 deaths. Ninety-seven per cent of the new cases will arise in persons over 45 years of age. Sixty-six per cent of the colorectal cancers and 79 per cent of the lung cancers will have metastasized by the time of diagnosis. Surgery and other treatment modalities will be used to treat 86 per cent of the colorectal cancers, but only 58 per cent of the lung cancers.

In contrast, cervical cancer has a much lower incidence and a much lower mortality rate, accounting for only 1 per cent of new cancer cases and cancer deaths in Rhode Island. Mortality from invasive cancer of the cervix has declined dramatically over the past 50 years, especially since the widespread application of screening using the Pap test. Nevertheless, cervical cancer remains a focal point of cancer control efforts because renewed screening activity, particularly with high-risk and hard-to-reach women, might further lower morbidity and mortality from the disease.

Cancer Screening: Who Benefits?

At present there is abundant evidence to support the routine use of screening tests for the early detection of cancer in selected age groups. This discussion will highlight the benefits and limitations of commonly utilized cancer detection tests that form the basis for general recommendations concerning the use of such tests in asymptomatic individuals. Since individuals may vary in terms of personal and family histories, risk factors, objectives, and budgets, general recommendations should be modified to take individual factors into account.

Breast Cancer

The goal of breast cancer screening is to detect early cancers prior to regional lymph node or distant metastases. Mammography has proven to be the most effective method for the early detection of breast cancer. As a result, screening centers are reporting a new pattern of stage distribution of breast cancer. Thus, in screening programs using mammography 40 per cent of the cancers discovered are $\leq$ 1 cm in diameter and 50 to 70 per cent of detected lesions are nonpalpable.[3] The well-known study conducted by the Health Insurance Plan of Greater New York demonstrated that through annual screening by medical history, physical examination, and mammography, the mortality from breast cancer could be reduced by almost 40 per cent in women over the age of 50. In contrast, no mortality reduction occurred in younger women, probably because the denser breast tissue in this age group made radiologic examination more difficult.[4] At present the value of breast cancer screening for women between the ages of 40 and 49 is less certain, but is currently being investigated in a randomized trial in Canada.

Self-examination of the breast is a simple, inexpensive, and safe procedure and seems to result in the detection of earlier cancers, particularly in high-risk groups. Additional studies are awaited before there is general agreement on the contribution of breast self-examination to the reduction of breast cancer mortality.[5]

The American Cancer Society (ACS) recommends a breast physical examination every three years for asymptomatic women ages 20 to 40 years and annually for women over 40. This examination should include inspection and palpation with the patient in three positions, that is, supine, oblique, and sitting. Mammography, using the lowest possible radiation doses, should be performed as a baseline study in women between ages 35 and 40, and annually in women over 50. Monthly breast self-examinations are encouraged for all women over age 20.[6]

Colorectal Cancer

The goal of colorectal cancer screening is the detection of an occult carcinoma prior to serosal penetration or regional lymph node metastasis, with a resultant increase in cure rate with surgery. Several screening modalities have been evaluated for their efficacy in detecting early cancers.

Guaiac impregnated slide tests for the detection of fecal occult blood have been incorporated into many screening programs. Successful utilization of these tests requires both patient compliance with a high-fiber, meat-free diet and careful follow-up. The percentage of patients with positive tests who are ultimately found to have carcinomas or adenomas increases with the age of the population, ranging from 15 per cent for individuals 40 to 49 years of age, to 60 per cent for those over 69 years.[7]

Digital rectal examination should be a part of any screening examination, not only to detect rectal carcinoma, but also prostatic cancer. Since the maximum depth of the examination is only 8 cm, procto-sigmoidoscopy has become a frequent method for the direct visualization of higher lesions. Since 50 per cent of carcinomas and adenomas are located in the distal 40 cm of bowel, a 65-cm flexible instrument is highly effective in the evaluation of the adequately prepared individual. Rigid proctoscopy, with a range of 16 to 25 cm, is much less effective and less well tolerated by patients.[8]

For evaluation of the entire colon, most observers recommend a double-contrast barium enema prior to fiberoptic colonoscopy because of the small, but definite false-negative rate of colonoscopy, which may fail to detect a lesion behind a sharply angulated segment of bowel.[9] Total colonoscopy, with biopsy of suspected lesions, should always follow, since up to 50 per cent of individuals may have synchronous adenomas and up to 5 per cent may have synchronous carcinomas.[10]

Many groups, including the American Cancer Society, recommend screening with annual digital rectal examinations for persons over age 40, with annual fecal occult blood testing for persons over age 50, and sigmoidoscopy every 3-5 years, after two negative studies one year apart, for persons over age 50.[6] These recommendations stem from the following estimates derived from available data: annual fecal occult blood testing alone may reduce colorectal cancer mortality about 30 per cent, a combination of fecal occult blood testing and flexible sigmoidoscopy every 5 years could reduce mortality 40 per cent, and annual fecal occult blood testing and barium enema every 5 years could reduce mortality about 60 per cent.[11]

Cervical Cancer

Although no randomized controlled trials have been conducted, a large body of evidence supports the value of the Pap smear for detecting preinvasive lesions of the cervix and early invasive cancers.[12] ACS guidelines recommend a three-year interval between Pap smears for women aged 20 to 70 years. This practice is estimated to yield a 70 to 95 per cent reduction in cervical cancer mortality. The natural behavior of cervical cancer supports the three-year interval since dysplasia precedes carcinoma *in situ* by five to ten years, and the average duration of carcinoma *in situ* is eight years. Currently, the most pressing problem regarding cervical cancer, in fact, is how to reach the women at highest risk, the estimated 20 per cent who have never had a Pap smear.

Assessment of Cancer Screening Activities

The Screening and Detection Working Group of the NCI has outlined a number of indicators which may be used to describe the scope of cancer screening activities in a given community. Some of these are outlined below:[13]

Breast Cancer: 1) What proportion of asymptomatic women, aged 50 to 70 years, have received physical examinations, mammography, or both for unsuspected breast cancer within the past year? 2) What proportion of high-risk women, aged 40 to 49 years, have received mammography within the past year? 3) What proportion of newly detected cases of breast cancer are diagnosed as carcinoma *in situ* or Stage I disease? 4) What proportion of women practice breast self-examination?

Colorectal Cancer: What proportion of men and women, aged 50 to 70 years, have received digital rectal examinations, fecal occult blood testing, and sigmoidoscopy within the past three years?

Cervical Cancer: What proportion of eligible women, aged 20 to 70 years, have received a Pap test within the past three years?

Recent national surveys conducted by the American Cancer Society in 1980 and 1983 have documented the frequency with which selected screening examinations are performed. Other than Pap tests in young women, the level of utilization of screening tests is generally low, and no trend toward increased utilization is apparent. The reasons for this poor acceptance are numerous and include such diverse factors as cost, inconvenience, discomfort, and lack of knowledge about the value of screening tests.[13]

A survey of cancer screening practices in Rhode Island has been conducted by the Roger Williams Cancer Center since October 1985. Over 400 adult men and women attending a comprehensive cancer screening program were questioned regarding the frequency of cancer screening practices using a written questionnaire. Frequencies for selected techniques are summarized by age and sex in Table 1. While cancer detection tests such as mammography, breast examination, and Pap tests have been performed with frequencies comparable to those reported nationally, it is pertinent that participants in a screening program are a self-selected group who may be more health-conscious than persons who do not attend such a program. Yet, there is considerable room for improvement, even in this group of motivated individuals.

Table 1. Frequency of Cancer Detection Tests among Participants of the Roger Williams Cancer Screening Program (N = 436)

Screening Technique	Men (N = 156) (%)	Women (N = 280) (%)
Breast physical examination, within last year		
aged 50-70 years	—	40%
Mammogram, within last year		
aged 40-49 years	—	23%
aged 50-70 years	—	21%
Breast self-examination, within last year		
aged 20-70 years	—	35%
Digital rectal examination, within last 3 years		
aged 50-70 years	53%	47%
Fecal occult blood testing, within last 3 years		
aged 50-70 years	38%	41%
Pap smear, within last 3 years		
aged 20-39 years	—	85%
aged 40-70 years	—	61%

NCI Objectives for Cancer Screening

The National Cancer Institute on the basis of available evidence recommends extension of cancer screening practices to achieve its prime objective for the year 2000: a 50 per cent reduction in the cancer mortality rate.[13] These recommendations can be summarized as follows:

1) The percentage of women aged 50 to 70 who have annual breast physical examinations plus mammography should be increased to 80 per cent from 45 per cent for physical examination alone and 15 per cent for mammography alone.

2) The percentages of women who have a cervical Pap smear every 3 years should be increased to 90 per cent from 79 per cent (for ages 20 to 39), and to 80 per cent from 57 per cent (for ages 40 to 70).

Cancer Screening in Rhode Island: Recent Efforts

Breast cancer has been the focus of a number of screening programs serving the Rhode Island community in recent years. Perhaps the earliest of these was the Breast Cancer Detection Demonstration Project at Rhode Island Hospital in Providence, cosponsored and funded by the National Cancer Institute and the American Cancer Society. Women were screened with a history, physical examination, mammography, and thermography annually for five years. Between 1974 and 1979, 9700 women had been screened and 95 breast cancers found. Of these, 32 were detected with mammography alone. At surgery, two-thirds of women did not have lymph-node involvement.[14]

In the spring of 1987 breast cancer screening programs were launched by several area hospitals, including Rhode Island Hospital and The Miriam Hospital. The ACS-sponsored programs offer education on breast self-examination and mammography at the reduced cost of $50. These programs will be of great import to Medicare beneficiaries, since Medicare does not pay for the use of a mammogram in the routine screening of asymptomatic women over age 50.

A comprehensive cancer screening program has been in progress at the Roger Williams Cancer Center since October 1985. Participants are screened for multiple cancer sites, including breast, colon, cervix, and skin using a medical history, physical examination, and selected screening tests, including Pap smears, mammography, fecal occult blood tests, and sigmoidoscopy, following American Cancer Society guidelines. Education is also provided in informal sessions on cancer risk factors, methods of prevention and early detection, and self-examination techniques. A more detailed description of the Roger Williams Cancer Screening Program will follow in the second part of this series.

Conclusions

Additional intensive cancer screening and education efforts are deemed appropriate for the Rhode Island community for the following reasons:

1) The rising cancer incidence and mortality rates for Rhode Island necessitate the timely implementation of cancer control measures statewide.

2) Abundant evidence exists to support the likelihood of mortality reduction through screening for breast and cervical cancer. Additional studies are awaited to prove conclusively a reduction in mortality through screening for colorectal cancer.

3) Rhode Islanders, as do their national counterparts, underutilize recommended screening measures.

4) Public interest and participation in previous cancer screening activities indicate the feasibility of implementing additional state-wide cancer control measuress.

Clearly, multiple factors contribute to participation in cancer screening programs. Those that facilitate participation include easy access to medical care, improved knowledge and attitudes related to cancer among health care professionals and the public at large, and third-party financing of screening activities. Successful allocation of resources to screening activities in Rhode Island will require careful definition and analysis of these factors.

Sufficient knowledge now exists to reduce the cancer death rate. This knowledge must be translated into action in the Rhode Island community. Delay will result in needless suffering and loss of life.

References

1. American Cancer Society: Cancer Statistics, 1987. CA 37 (1):15, 1987.
2. Rhode Island Cancer Control Program: Final Report of the Rhode Island Cancer Control Program to the Natinal Cancer Institute. Rhode Island Department of Health, Providence Rhode Island, June 1982.
3. Strax P: Strategy (motivation) for detection of early breast cancer. Cancer 46 (Suppl.):926-929, 1980.
4. Shapiro S, Venet W, Strax P, et al: Ten- to fourteen-year effect of screening on breast cancer mortality. JNCI 69:349-355, 1982.
5. Moore FD: Breast self-examination. N Engl J Med. 299:304-305, 1978.
6. American Cancer Society: Guidelines for the cancer-related checkup. Recommendations and rationale. CA 30 (4):194-240, 1980.
7. Winawer SJ and Sherlock P: Surveillance for colorectal cancer in average risk patients, familial high risk groups and in patients with adenomas. Cancer 50:2609-2614l, 1982.
8. Winman G, Berci G, and Parish J: Superiority of the flexible to the rigid sigmoidoscope. N Engl J Med 302:1011-1012, 1980.
9. Miller RE: Detection of colon carcinoma and the barium enema. JAMA 230:1195-1199, 1974.
10. Winawer SJ: Colon cancer. In Hunt, RH and Waye, JD (eds.): Colonoscopy. Chapman and Hall, England, 1981.
11. Eddy DM: Cost-effectiveness of colorectal cancer screening. In Levin B and Riddell RH (eds.): Frontiers in Gastrointestinal Cancer. Elsevier, New York, 1984.
12. American Cancer Society: Cancer of the cervix. CA 30:215-223, 1980.
13. National Cancer Institute Division of Cancer Prevention and Control: Cancer Control Objectives for the Nation: 1985-2000. NCI Monogr 2:3-93, 1986.
14. Fish FS and Scola FH: The Breast Cancer Detection Demonstration Project at Rhode Island Hospital. RI Med J 64:555-561, 1981.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

Thalidomide and D.E.S.

(They could happen again.)

Sometimes even the most promising drug may have unexpectedly adverse reactions in patients. Pre-market testing identifies most toxic drugs before release for patient-care use, but not all. Toxicity in some drugs can only be determined through adverse reactions detected among a larger number of patients over a longer period of time.

The plain truth is that a patient's health may be at risk. Adverse drug reactions cause death in approximately 30,000 patients annually in the United States alone. So, if you suspect an adverse drug reaction, please report it promptly. We may all live longer because you did.

The Adverse Drug Reaction Reporting Project

of the Rhode Island Department of Health

To report an ADR by phone, call **456-ADRS** weekdays between 9 and 5. To receive mailing forms and additional information, call the Health Department at 277-2901.

Acquired Immune Deficiency Syndrome (AIDS) and the Obstetrical Team

Strict Precautions Are Essential For All Exposed Personnel

Yusef Barcohana, MD

The acquired immune deficiency syndrome (AIDS) is a group of conditions that may reach epidemic proportions. The first clinical observation of AIDS was reported in 1981 by physicians in New York City and San Francisco.[1,2] The etiologic agent of AIDS was first isolated in 1983 by American and French investigators,[3,4] and named human T-cell lymphotropic virus type III (HTLV-III)/lymphadenopathy associated virus (LAV). This was recently renamed human immunodeficiency virus (HIV) which is a retrovirus causing life-time infection. HIV has been isolated from peripheral blood, lymph nodes, brain tissue, cerebrospinal fluid, urine, semen, cervical secretions, saliva, tears and human breast milk.[5-10]

Transmission of the virus may occur (1) via sexual contact, (2) via parenteral exposure to contaminated blood products, and (3) via the perinatal route (vertical spread) from mother to the child (transplacental, intrapartum exposure, and breast feeding).[11]

Yusef Barcohana, MD is Anesthesiologist-in-Chief with the Department of Anesthesia at Women and Infants Hospital of Rhode Island and a Clinical Associate Professor in Obstetrics and Gynecology (Anesthesiology) at Brown University, Division of Biology and Medicine, Providence, Rhode Island.

AIDS may be manifest as (1) overt AIDS, (2) AIDS-related complex (ARC), and (3) positive serum for HIV antibodies. Unlike many viral infections the presence of antibodies is not protective; rather it is indicative of an active infection with or without clinical manifestation.

The AIDS virus is not limited to one segment of society. Males, females, children, and fetuses of all races may become infected.

It is estimated that more than one million individuals are infected with the AIDS virus, and 20 per cent of these are women. Recently, Guinan and Hardy reported that the proportion of such women increased significantly between 1982 and 1986 from 12 to 25 per cent, and 80 per cent of these women are within childbearing ages. Eighty per cent of pediatric AIDS is linked to maternal transmission.[12]

The immunologic changes during pregnancy are similar to those described, although to a lesser degree than in patients with AIDS. In AIDS there is a change in the ratio of helper-to-suppressor cell (T4/T8). In pregnancy the T4/T8 ratio is also slightly depressed. This suggests that the pregnant state may favor the progression of HIV infection to ARC or AIDS.[13,14]

The histological changes seen in the lymph tissue, thymus gland and spleens of pregnant women parallel to a lesser degree the changes seen in AIDS patients. The immunological alterations in both pregnancy and AIDS may be

additive and pregnant patients with AIDS may become symptomatic with a higher mortality than non-pregnant women with AIDS. Most women infected with HIV are clinically well during pregnancy, but the fetus or newborn may be affected.

Embryopathy

A report from Italy revealed that 11 of 12 children born to HIV positive mothers were seropositive (91 per cent); five had AIDS (41 per cent) and two had ARC (16 per cent). Marion, et al reported a new morphologic syndrome associated with intrauterine HIV infection. Of 20 infants and children with positive serology tests to HIV, 75 per cent exhibited growth failure, 70 per cent microcephaly, and 50 per cent craniofacial abnormalities consisting of ocular hypertelorism; 75 per cent prominent box-like appearance of the forehead; 70 per cent flat nasal bridge; 65 per cent mild upward or downward obliguity of the eyes; 60 per cent long palpebral fissures with blue sclerae; 65 per cent short nose with flattened columella and well-formed, triangular philtrum; and 60 per cent patulous lips. These features constitute a new and distinct dysmorphic syndrome, the HIV embryopathy.[15] Obstetricians must educate their patients and inform them of the risk of transmitting the disease to their children if they become pregnant. The spread of AIDS among women created a concern for the obstetrical team (obstetricians, anesthesiologists, neonatologists, nurses, midwives, laboratory technicians, and environmental service personnel). AIDS patients are host to many opportunistic infections and may also have cytomegalovirus (CMV).[16] Therefore, pregnant health-care providers should not care for these patients as they may contract the infection. AIDS is a fatal disease, and all precautions should be undertaken to prevent its spread from patient to patient and from patient to health-care providers.

HIV is one of the most virulent infectious agents encountered in man. Transmission of AIDS by casual contact and contact with saliva, or airborne droplets, or by contamination of intact mucous membranes is unlikely, but has not yet been disproved. There are no contraindications to regional analgesia and anesthesia for gravid patients with ARC or patients who are seropositive for HIV antibodies. However, patients with overt AIDS should not receive regional anesthesia because the majority of such patients already have central nervous system and neurological involvement.[17]

Precautions against the transmission of hepatitis B also prevents transmission of HIV. As long as we do not have a mandatory AIDS testing program for pregnant women, then these precautions should be seriously extended to all the patients who are at high risk (intravenous users, prostitutes).

Precautions

Extraordinary precautions are absolutely necessary for all health care providers:

1. When the possibility of exposure to blood or other body fluids exists, gloves, masks, gowns, and eye coverings, especially at the time of delivery, cesarean section surgery, and the administration of anesthesia, as well as for infant resuscitation are mandatory.
2. Disposable items should be used for the care of these patients.
3. Sharp items (needles, scalpel blades, and other sharp instruments) should be handled with extraordinary care to prevent accidental injuries.
4. Needles and syringes should be disposable; needles should not be recapped or removed from syringes, but discarded into a puncture resistant container immediately after use.
5. Only disposable anesthesia equipment (mask, breathing circuit, laryngoscopes, and self-contained disposable CO_2 single use absorber) should be used.
6. All the reusable items should be placed in a Bio-Hazard® bag to be sterilized, then cleaned and sterilized again.
7. Hands and gloves contaminated by blood or other body fluids should be washed thoroughly with antiseptic agents.
8. In order to minimize the need for mouth-to-mouth resuscitation, mouth pieces, resuscitation bags, or Ambu® bags should be strategically located and available for use in all areas of the hospital.

Acknowledgment

I should like to thank Jane Dempsey, Nurse Epidemiologist at Women and Infants Hospital of Rhode Island, for providing information for this manuscript.

References

1 Centers for Disease Control. Kaposi's sarcoma and pneumocystis pneumonia among homosexual men — New York City and California. MMWR 30:305-308, 1981.

2 Centers for Disease Control. Pneumocystis pneumonia. Los Angeles. MMWR 30:250-252, 1981.

3 Gallo RC et al. Isolation of human T-cell leukemia virus in acquired immune deficiency syndrome (AIDS). Science 220:865-867, 1983.

4 Barre-Sinoussi et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 220:868-871, 1983.

5 Levy JA, Kaminsky LS, Morrow WJW, et al. Infection by the retrovirus associated with the acquired immunodeficiency syndrome. Ann Intern Med 103:694-699, 1985.

6 Ho DD, Rota TR, Schooley RT, et al. Isolation of HTLV-III from cerebrospinal fluid and neural tissues of patients with neurologic syndromes related to the acquired immunodeficiency syndrome. New Eng J Med 313:1493-1497, 1985.

7 Ho DD, Schooley RT, Rota TR, Kaplan JC and Flynn T. HTLV-III in the semen and blood of a healthy homosexual man. Science 226:451-453, 1984.

8 Groopman JE, Salahuddin SZ, Sarngadharan MG, et al. HTLV-III in saliva of people with AIDS-related complex and healthy homosexual men at risk for AIDS. Science 226:447-449, 1984.

9 Fujikawa LS, Salahuddin SZ, Palestine AG, Masur H, Nusenblatt RB and Gallo RC. Isolation of human T-lymphotropic virus type II from the tears of a patient with the acquired immunodeficiency syndrome. Lancet ii:529-530, 1985.

10 Thiry L, Sprecher-Goldberger S, Jonckheer T, et al. Isolation of AIDS virus from cell-free breast milk of three healthy virus carriers. Lancet ii:891-892, 1985.

11 Weber DJ, Redfield RR and Lemon SM. Acquired immunodeficiency syndrome: Epidemiology and significance for the obstretician and gynecologist. Am J Obstet Gynecol 155:235-240, 1986.

12 Guinan ME and Hardy A. Epidemiology of AIDS in women in the United States: 1981 through 1986. JAMA 257:2039-2042, 1987.

13 Sridama V, Pacini F, Yang SL et al. Decreased levels of helper T-cells: A possible cause of immunodeficiency in pregnancy. New Eng J Med 307:352-356, 1982.

14 Rhoads JL, Wright DC, Redfield RR and Burke DS. Chronic vaginal candidiasis in women with human immunodeficiency virus infection. JAMA 257:3105-3107, 1987.

15 Marion RW, Wiznia AA, Hutcheon RG and Rubinstein A. Human T-cell lymphotropic virus type III (HTLV-III) embryopathy. Am J Diseases in Children 140:638-640, 1986.

16 Drew WL, Conant MA, Miner RC et al. Cytomegalovirus and Kaposi's sarcoma in young homosexual men. Lancet 2:125-127, 1982.

17 Greene ER. Spinal and epidural anesthesia in patients with the acquired immunodeficiency syndrome. Anesth Analg 65:1089-1093, 1986.

101 Dudley Street
Providence, RI 02905

SECURITY

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY.... ANYWHERE

PLUS insurance for....
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

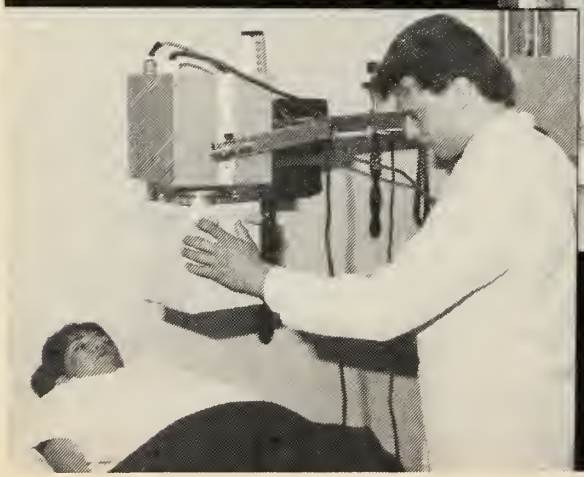
We've become the largest full service medical lab in Rhode Island... *because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

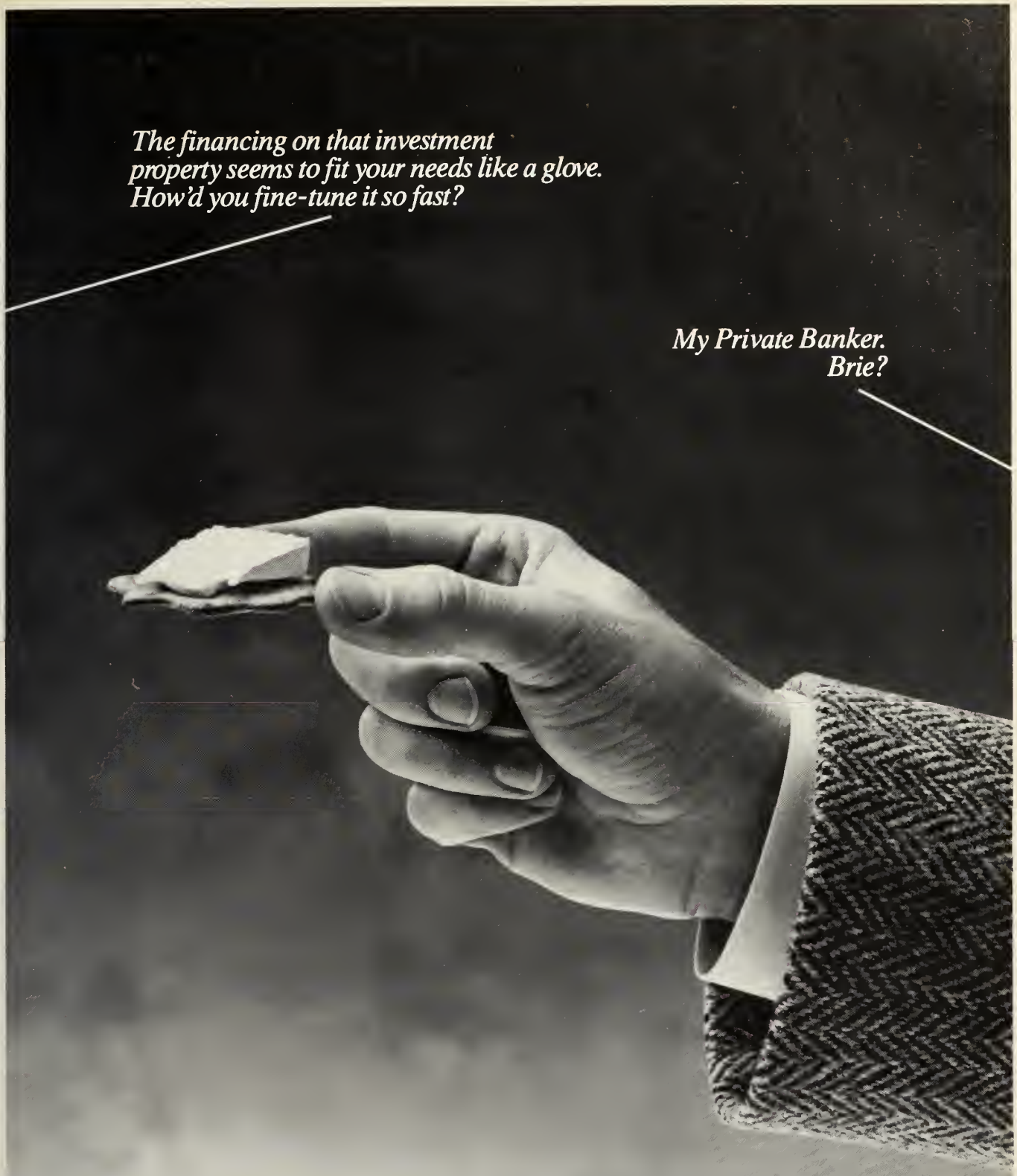
R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry Narragansett • West Warwick • Cumberland



When you have substantial assets, with an income to match, your Hospital Trust Private Banker can help further your financial well-being. Call the movers and shakers of Private Banking.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Equal Opportunity Lender

There are three ways to bil

STATEMENT
ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, USA

DOB
HOME PHONE
WORK PHONE
INS
INJURY DATE

JAMES SMITH
100 MAIN STREET
ANY CITY, U.S.A.

DATE	FAMILY MEMBER	PROFESSIONAL SERVICE	CHARGE	CREDITS Payments	CREDITS Adj.	CURRENT BALANCE
		BALANCE FORWARD →				60.
8/30/85	James	Bal. Forward				60.
9/3/85	" "	O.V	40.	Billed	9/5/85	100.
9/30/85		Medicare pmt/adj.		-45.	-8.	47.
10/10/85		patient pmt.		-7.		40.
10/25/85		Medicare pmt/adj.		-28.	-5.	7.
11/10/85		Pt pmt.		-7.		-0-
11/20/85	James	Int. O.V	40.	Billed	11/21/85	40.
12/6/85	James	Surgery	800.	Billed	12/20/85	840.
1/5/86		Medicare pmt/adj		-28.	-5.	807.
1/17/86		Court. adj.			-3.	804.
2/2/86		Medicare pmt/adj.		440.	250.	114.

PLEASE PAY AMOUNT IN THIS COLUMN

CA	Cast Application	C	Consultation	IP	Insurance Payment
CC	Cast Change	EC	Emergency Care	NC	No Charge
CK	Check	FS	Form Sent	OSA	Orthopedic Surgical Assistant
CR	Cast Removal	HVMC	Hosp Visit and Medical Care	OV	Office Visit
CRE	Credit	INJ	Injection	RPT	Report
CS	Cash			S	Surgery

THIS IS A COPY OF YOUR ACCOUNT AS IT APPEARS ON YOUR LEDGER CARD

THE OLD WAY.

Most patients are still getting fuzzy copies of hand-written ledger cards. No wonder they're confused about what they owe and why. No wonder they don't pay your bills.

THE INCOMPLETE WAY.

The same bill—computer-generated—only filled in with more questions than answers. How did the previous balance get to $804? What portion does the patient owe? Why do they owe it? Where's the detail?

STATEMENT

ANY CHARGES OR PAYMENTS RECEIVED AFTER THE DATE BELOW WILL APPEAR ON YOUR NEXT STATEMENT

ACCOUNT NUMBER	PAGE	DATE BILLED
12090	1	2/21/86

James Smith
100 Main Street
Any City, USA

AMOUNT REMITTED

ANY MEDICAL PRACTICE
ANY STREET
ANY CITY, U.S.A.

ANY CHANGE IN THE ABOVE ADDRESS SHOULD BE REPORTED TO OUR OFFICE

DETACH AND RETURN THIS PORTION WITH YOUR REMITTANCE TO THE ABOVE ADDRESS

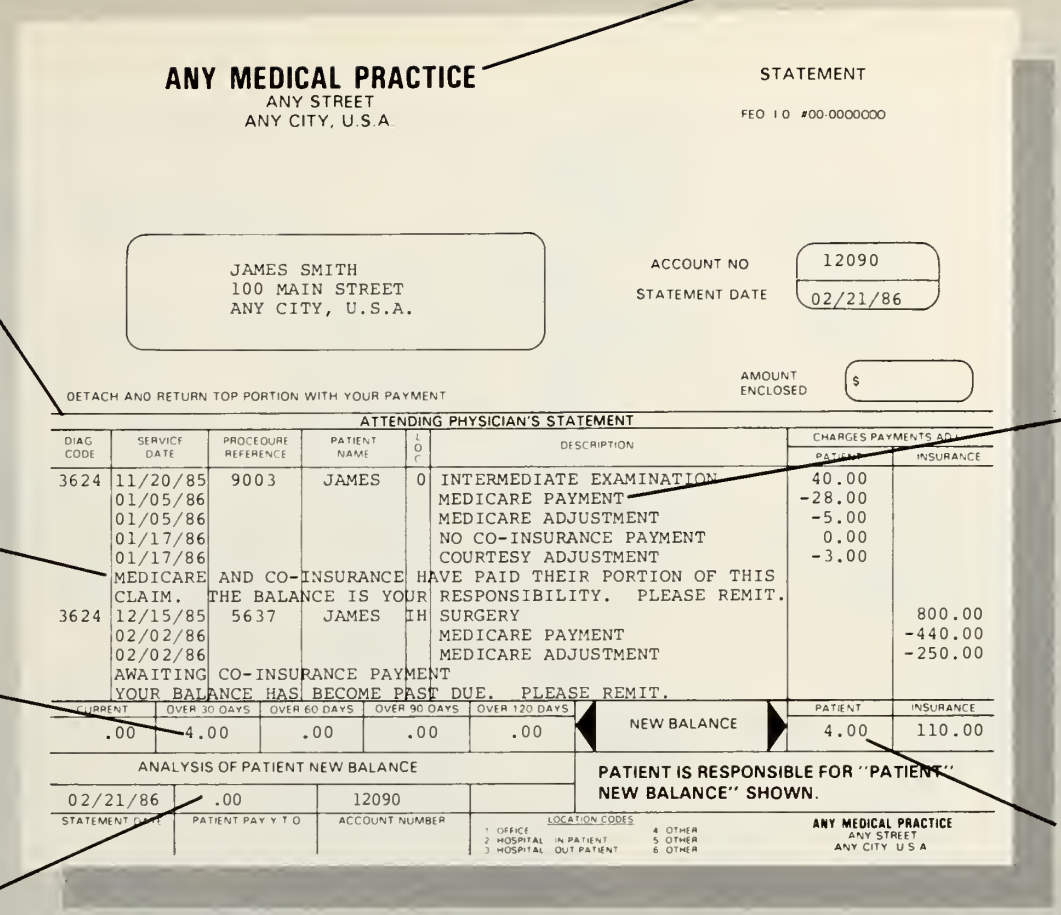
BILLED FROM 1-21-86
BILLED TO 2-20-86
DATE 2/21/8
ACCOUNT NUMBER 12090

MO	DAY	YR	DESCRIPTION	CHARGE	CREDIT
2	1	86	**Balance Forward**	804 00	
2	2	86	Medicare Payment		440 00
2	2	86	Medicare Adjustment		250 00

Your Account is past due.

CURRENT MO	OVER 1 MO	OVER 2 MO	OVER 3 MO	OVER 4 MO	TOTAL AMOUNT	TOTAL BALANCE
.00	.00	110 00	4 00	.00	114 00	114 00

your patients.



THE CONTEL WAY.

This bill says the same things as the bills on the left. Only better.

This bill *looks* like it comes from a professional. It's clear, concise, and detailed enough to stop those costly, time-consuming calls from impatient patients confused with hard-to-understand statements. And this detail is even more important with reimbursement policies changing so rapidly.

How do you send out a bill like this? Simply ask your nearby CONTEL Representative to install the medical business system that created it.

If all the system did was handle billing and insurance, that would be enough. But it manages *all* the business of your practice: management reporting, scheduling, claim tracking, medical records, word processing, financial accounting, and more.

Operating on the IBM family of personal computers and the powerful CONTEL computers, this medical business system is installed in over one thousand well-run practices.

Each system is installed by the same man who sells it, trains your people on it, supports it and guarantees it: The CONTEL Representative. He's your single source supplier, backed by Continental Telecom Inc.—the $4 billion telecommunications and data processing company.

IBM is a registered trademark of International Business Machines Corp.
CONTEL is a registered trademark of Continental Telecom Inc.

Call this toll-free number for the name of your nearest CONTEL Representative. Or mail in the coupon now. Learn why CONTEL Computer Systems is one of the nation's leading suppliers of practice management systems. And find out how your CONTEL Representative will make your practice almost perfect. **(401) 722-0303**

CONTEL Computer Systems
333 Elm Street • Dedham, MA 02026
(401) 722-0303

☐ Please rush me information on the CONTEL medical business system and the name of my nearest CONTEL Representative.

☐ Please have a CONTEL Representative call me right away.

NAME_____

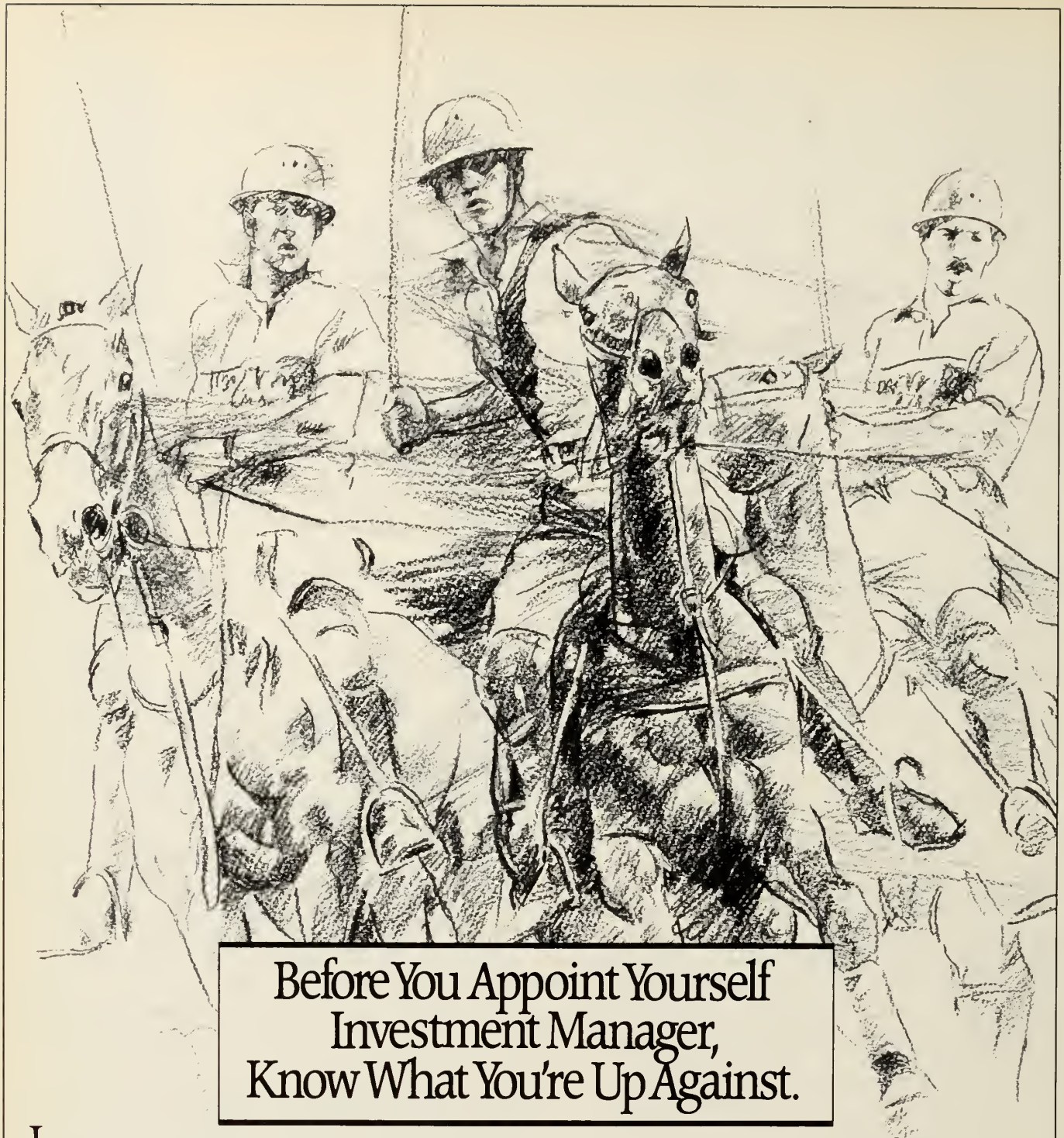
SPECIALTY_____

ADDRESS_____

CITY_____ STATE_____ ZIP_____

PHONE_____ PRESENT SYSTEM_____

Working hard in over 1,000 well-run practices



Before You Appoint Yourself Investment Manager, Know What You're Up Against.

Investment management today is a fast-paced, sophisticated field where only one thing really counts.

Performance.

Performance measured in terms of results and in terms of service.

As an experienced team of professionals dedicated full time to helping our clients achieve their financial goals, Hospital Trust's Investment Management and Trust Group has an enviable track record.

Specifically, we aim to provide a net return well in excess of the inflation rate. We do this, not by selling any specific type of investment, but rather by offering the widest possible range of strategies. Tailored to individual needs.

We have the diversity and depth to thoroughly think out the choices. Explore the possibilities. In stocks. In bonds. In real estate, precious metals and international investments.

No individual has quite this diversity of strengths.

So before you take on the role of investment manager, consider just how much horsepower it takes to do it right.

Then talk to the people with a proven track record. Hospital Trust.

For a uniquely objective evaluation of your investment needs or more information, call Gary Gherardini, Vice President, at 278-8730.

Hospital Trust

a BANK OF BOSTON company

INVESTMENT MANAGEMENT AND TRUST GROUP

A Rhode Island Philosopher (Elisha Bartlett)

The Annual Address, Delivered December 7, 1899

William Osler, MD

Rhode Island can boast of one great philosopher, one to whose flights in the empyrean neither Roger Williams nor any of her sons could soar, but the immortal Berkeley was only a transient guest in this State, waiting quietly and happily for the realization of his Eutopian schemes. Still he lived long enough in Rhode Island to make his name part of her history; long enough in America to make her the inspiration of his celebrated lines on the course of empire. Elisha Bartlett, teacher, philosopher, author, of whom I am about to speak, whom you may claim as the most distinguished physician of this State, has left no deep impression on your local history or institutions. Here he was born and educated, and to this, his home, he returned to die; but his busy life was spent in other fields, where to-day his memory is cherished more warmly than in the land of his birth.

I.

Born at Smithfield in 1804, Bartlett was singularly fortunate in his parents, who were members of the Society of Friends, strong, earnest souls, well endowed with graces of the head and of the heart. The gentle life, the zeal for practical righteousness and the simplicity of the faith of the followers of Fox, put a hall-mark on the sensitive youth which the rough usage of the world never obliterated. No account of Bartlett's early life and school-days exists — an index that they were happy and peaceful. We may read in his poem called "An Allegory," certain autobiographical details, transferring the

> "Meadow and field, and forest, dale and hill;
> Orchards, green hedgegrows, gardens, stately trees,"

from the old England which he describes to the banks of Narragansett Bay. Paraphrasing other parts of the poem, we may say that auspicious stars shone over his cradle with the kindliest light and promise, and amid the genial air of a New England home, goodness, truth and beauty were

William Osler, MD (1849-1919) was Professor of Medicine at Johns Hopkins University, Baltimore, MD.

Reprinted from Transactions of the Rhode Island Medical Society: *Vol. VI, pp 15-46, 1899.*

In this the 175th Anniversary year of the Rhode Island Medical Society, we are publishing from time to time significant papers by Rhode Island physicians or papers of historical interest appearing in the transactions of the Rhode Island Medical Society and the Rhode Island Medical Journal.

his portion. He tells of the wonder and delight stirred in his young soul by the thousand tales of "fairies and genii, giants, dwarfs and that redoubtable and valiant Jack who slew the giants." Then, as the days lengthened, he came under the spell of "The Arabian Nights" and of "Robinson Crusoe." Looking back in after years, he compared this hearty, wholesome life to some bounteous spring that wells up from the deep heart of the earth. Addison, Goldsmith and Washington Irving filled his soul with freshness like the dawn.

"And led by love and kindness, ran the hours
Their merry round till boyhood passed away."

In the ruder discipline and strife of school and college he grew to manhood with (as he expressed it) "a fine free healthfulness," and with faculties self-poised and balanced.

At Smithfield, at Uxbridge, and at a well-known Friends' institution in New York, Barlett obtained a very thorough preliminary education. Details of his medical course are not at hand, but after studying with Dr Willard, of Uxbridge, Drs Greene and Heywood, of Worcester, and Dr Levi Wheaton, of Providence, and attending medical lectures at Boston and at Providence, he took his doctor's degree at Brown University in 1826, a year before the untimely end of the medical department.[1]

In June, 1826, Bartlett sailed for Europe, and the letters to his sisters, which, with other Bartlett papers, have been kindly sent me by his nephew, the Hon Judge Bartlett of the New York Court of Appeals, give a delightful account of his year as a student abroad. He remained in Paris until December; then, in company with his fellow-student, Dr Southwick, he visited the chief cities of Italy, returning to Paris early in March. The month of May, 1827, was spent in London, and he sailed from Liverpool June 8th. Unfortunately the letters to his sisters contain very few references to his medical studies, but I have extracted a few memoranda from them.

Writing August 24, 1826, he says: "The celebrated Laennec died at his country residence on the 13th of the present month. The publication in 1819 of a new method of ascertaining diseases of the chest forms an era in the history of medicine. M Laennec fell a victim to one of those diseases the investigation of which by himself has enriched the field of science, contributed to the alleviation of human suffering, and giving his own name a high rank among the great and the good men of his age." He asked that this memorandum should appear in the Providence papers.

Writing September 4th, he speaks of attending every day at the Jardin des Plantes to hear the lectures of Cloquet and Cuvier.

One of the professors at the medical school, he says, looked more like a jolly stage driver or a good-natured, blustering butcher than anything else. "He lectures sometimes standing, and sometimes leaning against a post, or straddling over a high stool, flourishing a lancet in one hand and a snuff-box in the other, on the contents of which he is continually laying the most inordinate contributions. He wears during the time an old rusty looking black cap. The familiarity of the distinguished surgeons and physicians with their students struck me at first sight very forcibly, being in such perfect contrast to the proud port and haughty carriage of some of our New England professors. I wish they might step into the Hotel Dieu and La Charité and take a lesson or two of Boyer and Dupuytren, barons of the Empire, and two of the most distinguished surgeons in the world."

In the letter of October 10th, he says: "The public lectures opened this week, and we are continually engaged from half past six in the morning till bed time. Visits are made at all the hospitals by candle light, and a lecture delivered at most of them immediately after the visit."

He speaks of attending the lectures of Geoffrey St Hillaire, who, he says, "lectures very badly; his gestures, though he is a Frenchman, are exceedingly awkward, and he has a sing-song tone like that which one hears in a Methodist or Quaker preacher."

Bartlett probably acquired in Paris the three principles which Oliver Wendell Holmes said that he had learned: "Not to take authority when I can have facts; not to guess when I can know; not to think a man must take physic because he is sick."[2]

Strangely enough I find no reference in these Paris letters to the man of all others who influenced Bartlett most deeply. In Louis, even more than in Laennec, the young American students of that day found light and leading. The numerical method, based on a painstaking study of all the phenomena of disease in the words and in the dead-house, appealed with peculiar force to their practical minds, and Louis's brilliant observations on phthisis and on fevers constituted, as Bartlett remarked, a new and great era in the history of medical science. I cannot find any definite statement of Bartlett's relations with Louis

in 1826-27, at which period the latter was still working quietly at La Charité. His monograph on phthisis had been published in 1825, and had at once given him a reputation as one of the great lights of the French school. He was at this time very busy collecting material for his still more important work on typhoid fever, and it is scarcely possible that Bartlett could have frequented La Charité without meething the grave, unobtrusive student, who, with note book in hand, literally lived in the wards and in the dead-house. Secluded from the world, living as a voluntary assistant to Chomel in this quiet haven of observation, apart from the turbid seas of speculation which surged outside, Louis for seven years pursued his remarkable career. Whether or not Bartlett came into personal contact with him at this time cannot be decided. However this may be, subsequently the great French clinician became his model and his master, and to him he dedicated his first edition of the "Fevers," and his "Essay on the Philosophy of Medical Science."

For a young man of twenty-two, these letters — written offhand — show an unusually good literary style, and many incidental references indicate that he had received a general education much above the average. The strong Christian spirit which he felt all through life is already manifest, as may be gleaned from one or two expressions in the letters. Writing September 4, 1826, to his sisters, he refers to the death of a dear friend and her little sister: "There is a cheering consolation in the reflection that 'of such is the kingdom of heaven,' and that their spirits have gone in perfect and sinless purity to their home of bliss, and we may believe that they in their turn have become guardian angels to those who cherished and protected them here:

'They were their guardian angels here,
They guardian angels now to them.'"

In 1827, shortly after completing his twenty-third year, Bartlett settled at Lowell, then a town of only 3,500 inhabitants, but growing rapidly, owing to the establishment of numerous mills. This was his home for nearly twenty years, and to it, and later to Woonsocket, he returned in the intervals between his college work in different sections of the country. As Dr D C Patterson remarks, "He became at once the universal favorite, and began to take a deep interest in the physical welfare of the townsmen." In 1828 he delivered lectures before the Lowell Lyceum on contagious diseases, and he gave frequent popular lectures on sanitation and hygiene. In 1828 he was the orator on the Fourth of July. In 1836 he delivered a course of popular lectures on physiology.

Evidently Bartlett had the "grace of favor" in a remarkable degree. Bishop Clark pictures him in those days in the following words: "Some twenty-five years ago, I used to meet a young man in the town of Lowell, whose presence carried sunshine wherever he went; whose tenderness and skill relieved the darkness of many a chamber of sickness, and whom all the community were fast learning to love and honor. Life lay before him, full of promise; the delicate temper of his soul fitting him to the most exquisite enjoyment of all the pure delights of nature, and his cheerful temperament giving a genial and generous glow to the refined circles of which he was one of the chiefest ornaments."

When only thirty-two, before he had been in Lowell ten years, he was elected by a respectable majority as the first mayor of the city, and he was re-elected the following year. A letter from the Hon Caleb Cushing, dated April 20, 1841, gives us an idea of the estimate which a clear headed layman placed upon him. "Dr Bartlett enjoys in the city of Lowell the unqualified respect of that community, and its affectionate esteem, — respect and esteem due alike to his public relations to that city, as formerly its popular and useful chief magistrate, and at all times one of its most patriotic and valued citizens; to his unblemished integrity of character and amenity of deportment; to his eminence in his profession; to the endearments of private friendship; and in general to his talents, accomplishments, manners and principles."

To two interesting episodes in his life at Lowell I may refer at greater length. The rapid growth of the industries in Lowell had brought in from the surrounding country a very large number of young girls as operatives in the mills, and their physical and moral condition had been seriously impugned by writers in certain leading Boston papers. These charges were investigated in a most thorough way by Bartlett, who published in the *Lowell Courier* in 1839, and republished in pamphlet form (1841) his well-known "Vindication of the Character and Condition of the Females Employed in the Lowell Mills." This very strong paper, based on careful personal investigations, really proved to be what the title indicated. It did not, however, escape without adverse criticism, and among the Bartlett papers there is a review of the "Vindication" by a citizen of Lowell in 1842, which presents the other side of a picture,

by no means a pleasant one, of the prolonged hours of the operatives and their wretched life in boarding-houses.

One of the most interesting incidents of his life at this period was the reception to Dickens, whose visit to Lowell occurred during Dr Bartlett's mayoralty. In the "American Notes" Dickens speaks of the girls as "healthy in appearance, many of them remarkably so, and had the manners and deportment of young women, not of degraded brutes of burden." Oliver Wendell Holmes says, referring to this occasion: "I have been told a distinguished foreign visitor (Charles Dickens), who went through the whole length and breadth of the land, said that of all the many welcomes he received from statesmen renowned as orators, from men whose profession is eloquence, not one was so impressive and felicitous as that which was spoken by Dr Bartlett, then mayor of Lowell, our brother in the silent profession, which he graced with these unwonted accomplishments."

In 1840 he was elected to the Legislature of the State of Massachusetts and served two terms. In 1845 he was nominated by the Governor a member of the Board of Education of the State in the place of Jared Sparks. Holmes, who was familiar with Bartlett in this period of his career, has left on record the following charming description: "It is easy to recall his ever-welcome and gracious presence. On his expanded forehead no one could fail to trace the impress of a large and calm intelligence. In his most open and beaming smile none could help feeling the warmth of a heart which was the seat of all generous and kindly affections. When he spoke his tones were of singular softness, his thoughts came in chosen words, scholarlike, yet unpretending, often playful, always full of lively expressions, giving the idea of one that could be dangerously keen in his judgments, had he not kept his fastidiousness to himself, and his charity to sheathe the weakness of others. In familiar intercourse — and the writer of these paragraphs was once under the same roof with him for some months — no one could be more companionable and winning in all his ways. The little trials of life he took kindly and cheerily, turning into pleasantry the petty inconveniences which a less thoroughly good-natured man would have fretted over."

II.

For many years there was in this country a group of peripatetic teachers who like the Sophists of Greece, went from town to town, staying a year or two in each, or they divided their time between a winter session in a large city school and a summer term in a small country one. Among them Daniel Drake takes the precedence, as he made eleven moves in the course of his stirring and eventful life. Bartlett comes an easy second, as he taught in nine schools. Dunglison, T R Beck, Willard Parker, Alonzo Clark, the elder Gross, Austin Flint, Frank H Hamilton, and many others whom I could name, belonged to this group of wandering professors. The medical education of the day was almost exclusively theoretical; the teachers lectured for a short four months' session; there was a little dissection, a few major operations were witnessed, the fees were paid, examinations were held, and all was over. No wonder, under such conditions, that many of the most flourishing schools were found amid the sylvan groves of small country towns. In New England there were five schools in small towns, and in the State of New York the well-known country schools at Fairfield and Geneva. As there was not enough practice in the small places to go round, the teachers for the most part stayed only for the session, at the end of which it was not unusual for the major part of the faculty, with the students to migrate to another institution, where the lectures were repeated and the class graduated. T R Beck's introductory lecture, in 1824, at Fairfield, "On the Utility of Country Medical Institutions," pictures in glowing terms their advantages. One sentence brought to my mind the picture of a fine old doctor, on the Niagara peninsula, a graduate of Fairfield, who possibly may have listened to the very address. Dr Beck asks: "What is the clinical instruction of the country student? It is this — after attending a course of lectures on the several branches of medicine and becoming acquainted with their general bearing, he during the summer repairs to the office of a practitioner; attends him in his visits to his patients; views the diseases peculiar to the different districts; observes the treatment that situation or habits of life indicate and from day to day verifies the lessons he has received. Here then is a direct preparation for the life he intends to pursue." And I may say that it was just this training that made of my old friend one of the best general practitioners it has ever been my pleasure to know.

In the letters we can follow Bartlett's wanderings during the next twenty years, from the time of his appointment to one of the smallest of the schools to his final position as one of the chief ornaments of the leading school of New York.

In 1832 he held his first teaching position, that of professor of pathological anatomy and of materia medica in the Berkshire Medical Institute, at Pittsfield. The following is an extract from a letter to Dr John Orne Green, dated Pittsfield, November 25, 1833: "The character of the class is said to be superior even to that of last year. We have a large number of excellent students. Parker is as popular as ever, and Professor Childs has the credit of having improved very much in his manner of teaching. The members of the class are attentive to their studies, eager for knowledge, and regular in their attendance on the lectures. I have lectures, most of the time, twice a day, at 10 AM and at 2 PM I shall finish my course on materia medica by the middle of this week, and the remainder of my time will be occupied with lectures of medical jurisprudence and pathological anatomy. The commencement will be on Wednesday of week after next."

He held the chair at Pittsfield for eight sessions. Among his colleagues were Childs, Dewey and Willard Parker, who was a very special friend. In a letter of October 2, 1836, he says: "Parker, with his sunny face and his hearty welcome, was in a few minutes after my arrival. It does one good to meet such men."

In 1839 he was appointed to the chair of practice in Dartmouth College, Hanover, NH, the school founded by Nathan Smith in 1798. In a letter to his friend, Green, dated September 8th, he gives brief sketches of some of his colleagues, among them a delightful account of Oliver Wendell Holmes, then a young man of thirty. "Dr Holmes you know something of. As a teacher there is no doubt of his success, although he will not show himself during this his first course. He has his anatomy — some of it at least — to study as he goes on, and he has not yet got the whole hang of the lecture-room — he does not give himself his whole swing. His attainments in medical science are extensive and accurate, and his intellectual endowments are extraordinary. His mind is quick as lightning and sharp as a razor. His conversational powers are absolutely wonderful. His most striking mental peculiarities consist in a power of comprehensive and philosophical generalization on all subjects, and in a fecundity of illustration that is inexhaustible. His talk at table is all spontaneous, unpremeditated, and he pours himself forth — words and thoughts — in a perfect torrent. His wit and humor are quite lost in the prodigal exuberance of his thoughts and language." In this same letter is the following characteristic memorandum, illustrating his desire to see the school-houses beautified and adorned. "One word about the High School House. Pray, don't forget in the planning of the rooms my plan for some embellishments. Even if we should get some busts I do not know that niches would be any better than suitable stands or shelves. I hope we shall raise, by a fair, from five hundred to one thousand dollars for pictures, etc., for ornaments to the two principal rooms." It is quite possible that Bartlett lectured both at Woodstock and at Pittsfield, as the terms were purposely arranged so as not to clash, and in the catalogue of the Vermont Medical College, 1844, there is an advertisement of the Berkshire school. The names of Bartlett and Holmes occur only in the 1839-40 and 1840-41 announcements.

In 1841 he accepted the chair of the theory and practice of medicine in the Transylvania University, Lexington, at that time the strongest and best equipped school in the West.[3] On his way to Lexington he visited New York, Philadelphia, Washington and Baltimore, and in a letter to Green, of September 7, 1841, he gives an interesting account of the men he met in these cities. One item is of interest to Baltimoreans: "Day before yesterday I spent with Dr Nathan R Smith, at Baltimore, on my return from Washington. I found him very attentive and hospitable. He took me into his gig and went to see some of his patients. He has a pretty large surgical practice, and is, I should think, a man of excellent sound sense, industrious and devoted to his profession — not so *great* a man as his father, but a very capital good fellow. He speaks well of Lexington and the school — says it is the best appointed school in the country."

In his letters there are interesting descriptions of his life in Lexington, some of which are worth quoting: "In the school we are getting on very well. The class is of a good size, rather larger than last year, worth a little over $2,000, intelligent, attentive, well-behaved. I have given fifty-eight lectures, and we have just six weeks more. My own success has been good enough I think. So far as I have means of judging, my instruction is entirely satisfactory, to say the least. My colleagues — Dudley, you know, is the great man here. He has many peculiarities. He is very much pleased with me. He teaches singular doctrines, and follows, in many things, a practice very peculiar to himself. The other day he tied the common carotid before the class in an anastomosing aneurism in the orbit; patient from St Louis. Day before yesterday he cut for the stone; patient a

lad from Mississippi. He has two more cases of stone here for operation. He is exceedingly cautious; sends many patients, of all sorts, away without operation. Uses the bandage for everything almost in surgery — tart. ant. and starvation, or low diet, in most diseases. He had a pretty large property, 'a garden' as he calls it, of 150 acres or so, a mile from the city. Richardson, in obstetrics, boards with me, a plain common sense man, who fought a duel in early life with Dudley; has made a pretty large fortune here in practice, and now lives in the country eight miles or so from here, on a farm of 500 acres. The style of lecturing here is quite different from what it is in the East — more emphatic, more vehement. It is quite necessary to fall somewhat into the popular style. We stand, in the lecture room, on an open platform with only a little movable desk or table, on which to lay our notes. On the whole I like it better than being seated in a desk, as they are in Boston." (December 21, 1841.)

In March, 1843, he writes to Green that his receipts for the session have been more than $2,000. "There are a few good families who send for me, and I get occasionally a consultation. We never make a charge less than a dollar; and consultation visits in ordinary cases — the first visit — are $5.00. These few enable me situated as I am, to make even a small and easy business somewhat profitable. I have made one visit twenty-five miles distant, for which the fee was $25; and I saw a second patient, at the same time, incidentally, for $5.00 more. You see from all this, that my place gives me rather more money than I could earn in Lowell, for a much smaller amount of responsibility and labor. I have hardly, indeed, been called out of bed during the winter. In a business point of view I feel quite content with my situation."

From an interesting account of a consultation in the country we can gather how the planters of those days did their own doctoring: "Col Anderson belongs to a class of men, pretty large, I think, in this State, — rather rough, with a limited school education, but intelligent, shrewd, clearheaded, and enterprising. He has a farm, entirely away from any travelled road, of 500 acres; but his principal business is that of bagging and soap manufacturing, his farm serving only to feed his family. This consists of about one hundred, eighty or more of which are his negroes. He has no physician, whom he is willing to trust, nearer than Lexington; and in nearly all common acute diseases treats the patient himself. His daughter, Mrs Breck, was seized with acute pleurisy, soon after miscarriage, and her father had bled her twice, pretty freely, and given calomel and antimony, before any physician had seen her. He had followed the same course a year ago in the case of his wife." (February 18, 1844.)

In the same letter he says: "Typhoid fever has been very widely prevalent in many parts of Kentucky for the past year. There were, it is said, 200 deaths in an adjacent county last summer and fall. It is evidently the common fever of this country, with all the features so familiar to us at the East."

In the autumn of 1844 he accepted the chair of the theory and practice of medicine at the University of Maryland. Among the letters I find but one from Baltimore, and that is to Oliver Wendell Holmes about a review of his book, "The Philosophy of Medical Science," which had appeared that year.

In 1844 he accepted the chair of materia medica and obstetrics in the Vermont Medical College, the session of which began in March and continued for thirteen weeks. Among his colleagues were Alonzo Clark, Palmer and Edward M Moore and later John C Dalton. Bartlett's name occurs in the catalogues of the school until 1854, the year before his death. In May, 1845, he and Mrs Bartlett sailed for Europe. In a letter to Green, July 12th, there is an interesting reference to Louis and James Jackson, Jr. "I have seen a good deal of Louis, who has been very civil and attentive. I dined with him soon after my arrival, and met there, amongst others, Leuset and Grisolle, two of his most intimate medical friends that he does not speak of young Jackson — *ce pauvre Jackson,* as he calls him. He told me, with a great deal of feeling, that Jackson, the last night that he spent in Paris, wrote him a letter from his hotel, which was moistened with his tears, and that he thought Jackson was almost as much attached to him as to his father." In another letter he speaks, too, of his very cordial reception by Louis.

They spent the winter on the Continent, traveling about, chiefly in Italy, and in the spring went to London. In a letter dated June 17, 1846, there is an interesting sketch of a magnetic séance at the house of Professor Elliotson, of University College, who subsequently came to such a grief over hypnotism. "And then he ran full tilt off upon his hobby, 'animal magnetism,' calling it one of the most sacred and holy of all subjects, one of the greatest truths, and so on. Dr Forbes, the editor, he spoke of as 'a wretch,' all because the doctor has shown up some of Elliotson's mag-

netic operations. Dr E afterwards invited me to see some magnetic phenomena at his house. I went about 3 o'clock in the afternoon, and found his spacious and elegant drawing-room quite filled with well-dressed gentlemen and ladies, assembled for the same purpose. The doctor had two subjects, one a young, delicate looking girl, and the other a damsel of a certain age, upon whom he performed the standard and stereotyped experiments — putting them into the magnetic sleep, stiffening their limbs, leading them round the room with a common magnetic, exciting their phrenological organs, and so on. I can only say that I was not specially delighted with Elliotson's manner, and that if I was to choose a man by whom I should swear, without using my own eyes, certainly it would not be him."

In the same letter he speaks of having seen a great deal of Forbes, editor of the *Medico-Chirurgical Review;* of Marshall Hall, of Walshe, "a young man and a good fellow;" of Sir Henry Holland, and of that interesting American physician, who lived so long in England, Dr Boott, and of Dr Southwood Smith, at the Fever Hospital.

On his return from Europe we find him during the session of 1846-47 in his old chair at Lexington, whence he writes on March 18, 1847, to his friend Green, from which a paragraph relating to the second edition of his book on "Fevers" may be quoted: "I have been drudging away all winter at my second edition. I do not feel any great interest in it, though I hope and intend to make a good book of it. The first edition, for a monograph, has sold very well, mostly at the South and West; so well at least that Lea & Blanchard propose publishing the second edition and paying also something for the right to do so."

The next sessions of 1847-48-49 were spent at the Transylvania University. In the spring of 1848 there is a letter from Pliny Earle, dated April 16th, saying that he had received a catalogue of the Medical Department of Transylvania University, from which he had received his first intimation of Bartlett's resignation of the professorship. He asks Bartlett's advice as to the propriety of applying for the position.

On March 13, 1849, he received the appointment as professor of the theory and practice of medicine in the University of Louisville. At this time, in a letter from Dr J Cobb, we have the first intimation in the letters of ill health, as there is the sentence: "Accept my best wishes for your complete restoration to health." The University of Louisville had drawn heavily upon the classes of the other Western schools, chiefly at the expense of Lexington, and the Faculty when Bartlett joined it was very strong, comprising such well-known men as the elder Gross, the elder Yandell, Rogers, Benjamin Silliman, Jr, and Palmer.

The condition of medical politics at that time in the town of Louisville was not satisfactory, and a new school had been started in opposition to the University, and among the Bartlett letters are a number from the elder Yandell which show a state of very high tension. Bartlett spent but one session in Louisville. He and Gross accepted chairs in the University of New York. The appointment of the former to the chair of the institutes and practice of medicine is dated September 19, 1850. From some remarks in a letter from Yandell it is evident that Bartlett did not find the position in New York very congenial. Gross found his still less so, and returned to Louisville the following year. J W Draper, the strong man of the University School, had secured Bartlett and in a letter dated August 12, 1850, he promised him a salary of at least $3,500. The same letter shows how thoroughly private were the medical schools of that day: "It perhaps may be proper to repeat what is the condition of the real estate — The college building is owned equally by the six professors. Its estimated value when Dr Dickson left us in the spring was $78,600, and there is a mortgage upon it of $48,000, bearing interest of six per cent. Excluding this mortgage the share of each professor is therefore $5,000, and a mutual covenant exists among us that on the retirement or decease of one of the Faculty his investment shall be restored to him or his heirs — the newcomer starting in all respects in the position he occupied."

During these years Bartlett seems to have been very busy at work at the microscope, and there is a letter from Alonzo Clark, dated June 15, 1848, descriptive of a fine new Oberhauser (the Zeiss of that day), and in 1851 there is an interesting letter from Jeffries Wyman, giving a list of the most important works on invertebrate zoölogy.

Among his colleagues in the University were Draper, Martyn Paine and Patterson. Things do not seem to have worked very smoothly. In the spring of 1851 overtures were made to him from the College of Physicians and Surgeons of New York, in which Faculty were his warm friends, Alonzo Clark and Willard Parker, and he was elected to the chair of materia medica and medical jurisprudence in the following year, in 1852. Here he lectured during the next two sessions

until compelled by ill health to retire.

I may fittingly conclude this section of my address with a sentence from a sketch of his life by his friend Elisha Huntington: "Never was the professor's chair more gracefully filled than by Dr Bartlett. His urbane and courteous manners, his native and simple eloquence, his remarkable power of illustration, the singular beauty and sweetness of his style, all combined to render him one of the most popular and attractive of lecturers. The driest and most barren subject, under his touch, became instinct with life and interest, and the path, in which the traveler looked to meet with briers and weeds only, he was surprised and delighted to find strewn with flowers, beautiful and fragrant. There was a magic about the man you could not withstand; a fascination you could not resist."

III.

Bartlett began his career as a medical writer with the *Monthly Journal of Medical Literature and American Medical Students' Gazette,* only three numbers of which were issued. He says in the introductory address, dated October 15, 1831, that there are plenty of practical journals of high character and extensive circulation, but he wishes to see one devoted to "medical history, medical literature, accounts of medical institutions and hospitals, medical biography, including sketches of the character, lives and writings of the chief masters of our art, and of all such as have in any way influenced its destinies and left the deep traces of their labors on its history. . . . To the medical student and the young practitioner, to all those who aspire to any higher acquisitions than the knowledge that calomel purges and salivates, and that tartarized antimony occasions vomiting, who are not willing to rest supinely satisfied in a routine familiarity with doses and symptoms — a familiarity which practice and habit render in the end almost mechanical — we cannot but think these matters must be interesting." And he adds: "The devotion of an occasional hour to such pursuits must have a tendency to enlarge and liberalize the mind. It will help to keep alive and stimulate in the young medical scholar the sometimes flagging energies of study. By calling his attention and directing his desires to high standards of acquisition and excellence, it will urge him on towards their attainment. Delightful and fascinating, in many respects, as the study of his profession may be to him, there are many hours which must be occupied with mental and bodily drudgery. He must make what to others would be loathsomeness pleasure to himself. Amid the wear and tear, the toil and fatigue of such pursuits, he needs at times some intellectual recreation and stimulus, and where can he find one pleasanter or more appropriate than in surveying the career, and studying the characters of those who have trodden before him the same laborious path, and who have followed it on to its high and bright consummation? If our profession ever vindicates its legitimate claim to the appellation of liberal, it must be cultivated with some other than the single aim of obtaining patients for the sole purpose of getting for services rendered an equivalent in fees."

In the first number there is a statement that on a future occasion the *Journal* will give a "detailed consideration of the character of the old physician of Cos — the venerable father of physic, and of the reform which he effected in medical science," a promise which was not fulfilled to the profession for many years, as Bartlett's well-known lecture on Hippocrates, the last, indeed, of his professional writings, was not issued until 1852. The literature of science, its philosophy, its history, the history of the lives and labors of the founders and cultivators — these he believed it important for the student to cultivate.

Among the articles in these three numbers there are some of special merit. One signed S N, "On the Claims of Medicine to the Character of Certainty," may have suggested to Bartlett in his well-known essay, "On the Degree of Certainty in Medicine." The enterprise was not a success, and as Bartlett had said in his introductory address, "of all *weakly* things we most heartily pity weakly periodicals," he had the good sense after three numbers had been issued to give up a publication which the profession did not sustain.

In July, 1832, he became associated with A L Pierson and J B Flint in a much more pretentious and important journal, the *Medical Magazine,* a monthly publication which continued for three years. It was a very well conducted periodical, with excellent original articles and strongly written editorials. John D Fisher's original paper on the cephalic brain murmur occurs in Volume II, and in the same one is an excellent paper by E Hale, Jr, on the typhoid fever of this climate, which is of special interest as containing very accurate statements of the differences between the common New England autumnal fever and the typhus as described by Armstrong and Smith. There are also reports of three autopsies giving an account of ulceration in the small intestine, among the first to be published in this country.

There are in addition numerous well-written critical reviews. Among the latter is one of the most virulent productions of that most virulent of men, Dr Charles Caldwell. It is entitled "Medical Language of Literature." I have heard it said in Philadelphia that Dr Samuel Jackson never forgave the bitterness of the attack in it upon his "Principles of Medicine."

In Volume III there was the interesting announcement that a dollar a page would be paid for all original communications.

In 1831 appeared a little work entitled, "Sketches of the Character and Writings of Eminent Living Surgeons and Physicians of Paris," translated from the French of J L H Peisse. Of the nine lives, those of Dupuytren and Broussais are still of interest to us, and I know of no work in English from which one can get a better insight into the history of medicine in Paris in the early part of this century. One little sentence in the translator's preface is worth quoting: "After making all reasonable allowance for natural tact or talent, and for the facilities and advantages of instruction to be had in extensive medical establishments, it will be found that *study*, intense, untiring, unremitted *study*, is the only foundation of professional worth and distinction."

A great stimulus had been given to the study of phrenology by the visit of Spurzheim to this country. He gave a course of six lectures on the anatomy of the brain and spinal cord at one of the apartments of the Medical College in September of that year, and subsequently a popular course of lectures on phrenology. In 1832 he died in Boston of typhus fever. His brain, it is stated, was in the possession of the Boston Phrenological Society, before which, in January, 1838, Bartlett gave an interesting address on scientific phrenology.

In 1839 Bartlett edited "Paley's Natural Theology," that delightful book, dear especially to those of us who were trained in religious colleges. To some of us at least the freshness of the natural theology, which in Paley's hands was really a delightful commentary on anatomy and physiology, was a happy change from artificial theology, or even from the "Horae Paulinae" of the same author.

Bartlett's claim to remembrance, so far as his medical writings are concerned, rests mainly on his work on "Fevers" issued in 1842, and subsequent editions in the years 1847, 1852 and 1857. It remains one of the most notable of contributions of American physicians to the subject. Between the time of Bartlett's visit to Paris and 1840, a group of students had studied under Louis, and had returned to this country thoroughly familiar with typhoid fever, the prevalent form in the French capital at that time. In another place[4] I have told in detail how largely through their labors the profession learned to recognize the essential differences between the two prevalent forms of fever, typhoid and typhus. The writings on fever chiefly accessible to American readers at that day were the English works of Fordyce, Armstrong, Southwood Smith and Tweedie, in which, as Bartlett says, "they describe a fever or form of fever (that is typhus) rarely met with in this country," and the writings did not actually represent the state of our knowledge upon the subject. Indeed, for a number of years later a chaotic condition of mind prevailed among the writers in Great Britain, and it was not until 1949-50 that William Jenner, by a fresh series of accurate observations, brought the British medical opinion into line. As the *British and Foreign Medico-Chirurgical Review,* in a most complimentary notice of Bartlett's work, says, "A history of British fevers such as Louis has furnished to France, or such as given in the volume under discussion, did not exist." Still, even at that date, 1844, the *Review* expressed the ultra-conservative opinion held in England, that the common continued fever, or the low nervous fever of Huxham, was only a mild form of typhus fever. The work is dedicated to his friends, James Jackson, of Boston, and W W Gerhard, of Philadelphia; as he states, "a history of two diseases, many points of which they, especially among his own countrymen, having diligently and successfully studied and illustrated."

As to the work itself, the interest to-day rests chiefly with the remarkably accurate picture which is given of typhoid fever — a picture the main outlines of which are as well and firmly drawn as in any work which has appeared since. It is written with great clearness, in logical order, and he shows on every page an accurate acquaintance with the literature of the day, and, as the author of the review already mentioned remarks, a knowledge also of that best of books, the book of nature.

The practical character of Bartlett's mind is indicated by the briefness with which he discusses the favorite topic of the day, namely, the theory of fever. He acknowledged at the outset that the materials for any satisfactory theory of typhoid fever did not exist. He went so far as to claim that the fundamental primary alteration was in the blood, and that the local lesion was really

secondary, and he refers to the prevalent theory of fever as "wholly a creation of fancy; the offspring of a false generalization and of a spurious philosophy. What then can its theory be but the shadow of a shade?" This work immediately placed Bartlett in the front rank of American physicians of the day. It had a powerful influence on the profession of the country. Among his letters there is an interesting and characteristic one from James Jackson, already referred to in the dedication. Acknowledging the receipt of a copy, he says: "I am now writing to express to you the great satisfaction the book has given me. I think that it entirely answers the end that you proposed. It, in fact, translates to the common reader, in a most clear style and lucid method, the acquisitions which science has made on its subjects within the last few years. Nowhere else can the same comprehensive view of those subjects be found. What may be the conclusions of medical men in regard to essential fever twenty years hence I would not pretend to say. It is certain their views have changed very much within a shorter period, and if new discoveries are made in ten years to come I doubt not you will be ready to change yours. We must take to-day the truth so far as we know it, and add to it day by day as we learn more."

It is evident from his letters that the success of the work on fevers was a great gratification to Dr Bartlett. The second edition was issued in 1847, and while the history of typhoid and typhus fever remained much in the same state, with certain additions and developments, the subject of periodical and yellow fevers were greatly extended. The third edition was issued in 1852. The fourth edition was edited by Bartlett's friend Alonzo Clark, of New York. The dedication of the second, third and fourth editions was to Dr John Orne Green, of Lowell, "with whom the early and active part of the writer's life was passed; in a personal friendship which no cloud, for a single moment, ever shadowed or chilled; and in a professional intercourse whose delightful harmony no selfish interest nor personal jealousy ever disturbed."

From every standpoint "Bartlett on Fevers" may be regarded as one of the most successful medical works issued from the medical press and it richly deserves the comment of the distinguished editor of the fourth edition: "The question may be fairly raised whether any book in our profession illustrates more clearly the beauties of sound reasoning and the advantages of vigorous generalization from carefully selected facts. Certainly no author ever brought to his labor a more high-minded purpose of representing the truth in its simplicity and in its fullness, while few have been possessed of higher gifts to discern, and gracefully to exhibit it."

"An Essay on the Philosophy of Medicine," 1844, a classic in American medical literature, is the most characteristic of Bartlett's works, and the one to which in the future students will turn most often, since it represents one of the most successful attempts to apply the principles of deductive reasoning to medicine, and it moreover illustrates the mental attitude of an acute and thoughtful observer in the middle of the century. The work consists of two parts: in the first science is defined and its canons laid down. Ascertained facts, with their relations to others, obtained by observation or experience, and generalized into laws and principles — this constitutes science. He dwells upon the hurtfulness of theories, and sketches in an interesting manner Newton's position as an observer and as a theorist: "If he (Newton) bowed at any time or in any degree his strong neck to the yoke of hypothesis, it was always with a perfect consciousness of his ability at will to shake it off, as the lion shakes the dewdrop from his mane." He quotes from Sir Humphrey Davey: "When I consider the variety of theories that may be formed on the slender foundation of one or two facts, I am convinced that it is the business of the true philosopher to avoid them altogether."

The five primary propositions with which the second part opens contain the pith of the argument:

Proposition First. — All medical science consists in ascertaining facts, or phenomena, or events; with their relations to other facts, or phenomena, or events; the whole classified and arranged.

Proposition Second. — Each separate class of facts, phenomena, and events, with their relationships, constituting, as far as they go, medical science, can be ascertained in only one way; and that is by observation, or experience. They cannot be deduced, or inferred, from any other class of facts, phenomena, events, or relationships, by any process of induction, or reasoning, independent of observation.

Proposition Third. — An absolute law, or principle, of medical science consists in an absolute and rigorous generalization of some of the facts, phenomena, events, or relationships, by the sum of which the science is constituted. The actual ascertainable laws, or principles, of medical science are, for the most part, not absolute but ap-

proximative.

Proposition Fourth. Medical doctrines, as they are called, are, in most instances, hypothetical explanations, or interpretations, merely, of the ascertained phenomena, and their relationships, of medical science. These explanations consist of certain other assumed and unascertained phenomena and relationships. They do not constitute a legitimate element of medical science. All medical science is absolutely independent of these explanations.

Proposition Fifth. — Diseases, like all other objects of natural history, are susceptible of classification and arrangement. This classification and arrangement will be natural and perfect just in proportion to the number, the importance, and the degree of the similarities and the dissimilarities between the diseases themselves.

Bartlett is the strongest American interpreter of the modern French school of medical observation, which "is characterized by its strict adherence to the study and analysis of morbid phenomena and their relationships; by the accuracy, the positiveness, and the minute detail which it has carried into this study and analysis; and by its rejection as an essential or legitimate element of science of all *a priori* reasoning or speculation. The spirit which animates and guides and moves it is expressed in the saying of Rosseau, 'that all science is in the facts or phenomena of nature and their relationships, and not in the mind of man, which discovers and interprets them.' It is the true *protestant* school of medicine. It either rejects as apocryphal, or holds as of no binding authority, all the traditions of the fathers, unless they are sustained and sanctioned by its own experience."

There are weak points in his arguments, some of which are well pointed out in an able article in the *British and Foreign Medico-Chirurgical Review* (July, 1845), but it is the work of a strong and thoughtful mind, and for a time, at least, it had a powerful influence in the profession. A contemporary writer, S H Dickson,[5] speaks of it in the following terms: "It was particularly well-timed, and addressed effectively to the requirements of the profession, at the period of its publication. It breathes a spirit of thoughtful and considerate skepticism, which was then needed to temper the headlong habit of confident polypharmacy prevalent over our country.

. . . When addressed, however, by Bartlett, on this side of the Atlantic, and on the other by Forbes, he (the orthodox disciple) stopped to listen and consider. These gifted men spoke with authority; they pleaded impressively, eloquently, wisely. If, in the natural ardor of controversy, they went somewhat too far, let that slight fault be forgiven for the great good they accomplished. Nay, let them be honored for the courage and frankness with which they attacked prevalent error, and risked their popularity and position by assailing modes of practice rendered familiar by custom, and everywhere adopted and trusted to."

In 1848 appeared one of Bartlett's most characteristic works, a little volume of eighty-four pages, entitled, "An Inquiry into the Degree of Certainty of Medicine, and into the Nature and Extent of its Power over Disease." The iconoclastic studies of Louis and certain of the Paris physicians, and the advocacy of expectancy by the leaders of the Vienna school, had between 1830 and 1850 disturbed the profession not a little, and in 1846 appeared an article by Dr Forbes, in which, as Bartlett said, were drawn "in strong and exaggerated colors the manifold imperfections of medical science and the discouraging uncertainties of medical art." These circumstances had combined to shake and disturb the general confidence in the profession, with the effect that "the hold which medicine has so long had upon the popular mind is loosened; there is a widespread skepticism as to its power of curing diseases, and men are everywhere to be found who deny its pretensions as a science, and reject the benefits and blessings which it proffers them as an art." To Bartlett it appeared high time to speak a clear and earnest word for the science which we study and teach, and for the art which we inculcate and practise, and in this essay he set himself the task of vindicating the claims of medicine to the regard and confidence of mankind. In his endeavor "to show how far and with what measure of certainty and of constancy we are able to control, to mitigate and to remove disease" Bartlett occupied at the outset very advanced ground for that date. We must remember that the general body of the profession had the most implicit confidence in drugs, and polypharmacy was almost as much in vogue as in the seventeenth and eighteenth centuries. The reception of the essay in certain quarters indicates how shocking its tone appeared to some of the staid old conservatives of the day. I came across a review of it in the *Medical Examiner*, November, 1848, from which I give the following extract: "This is a curious production, the like of which we have seldom seen from the pen of any one who had passed the age of a sophomore.

What makes it more remarkable is the circumstance that the writer is a gentleman of education and experience and the author of works which have given him a wide reputation." The force of the rebound sufficiently indicates the intensity with which the attack was felt. Bartlett's position, however, reminds one somewhat of the sermon of the liberal Scotch Presbyterian on "things which cannot be shaken," in which he proceeded at the outset to shake off three-fourths of the cherished beliefs of Evangelical Christianity.

After a preliminary discussion on anatomy and physiology, and on the remarkable rapidity with which these sciences were progressing, he proceeds to speak of the state of pathology and therapeutics as illustrated in the well-known disease pneumonia. Time will not permit me to do more than to refer to the result of his analysis of the evidence. He classifies the cases into, first, those which terminate naturally and spontaneously, quite independent of any active medical treatment, a proportion "probably large"; second, a group which will terminate fatally notwithstanding any assistance which art may furnish; they are, as Sir Gilbert Blane said of the worst forms of yellow fever, "determinedly fatal"; and, finally, a third class "not tending necessarily either in one direction or the other," in which the issue depends upon the treatment of the disease. "In these cases, art, judiciously applied, saves the life of the patient; the issue of the cases, in death or recovery, is dependent upon the treatment of the disease." Then follows a discussion on the nature and limits of the medical art in the various groups of diseases, and he concludes with a section on the triumphs of preventive medicine.

The initials "A S" at the end of a review in the *American Journal of the Medical Sciences,* October, 1848, enable us to estimate the impression which the book made upon a kindred spirit. Professor Alfred Stillé, of the University of Pennsylvania (still with us, I am happy to say), wrote, "He has done a good work, a work for which he deserves the respect and gratitude of the medical profession, and of all sound-hearted men, whatever their pursuits, who fight under the banner of truth, and are the sworn foes of all imposture, the determined opponents of all error."

At times and in degrees differing with our temperaments, there come upon us bouts of depression, when we feel that the battle has been lost, and that to fight longer is not worth the effort, periods when, amid the weariness, the fever and the fret of daily practice, things have gone against us; we have been misunderstood by patients, our motives have been wrongly interpreted, and smitten perhaps in the house of our friends, the worries of heart to which we doctors are so subject, makes us feel bitterly the uncertainties of medicine as a profession, and times make us despair of its future. In a voice that one may trust Bartlett concludes his inquiry with these memorable words, which I quote, in the hope that they may soothe the heartache of any pessimistic brother: "There is no process which can reckon up the amount of good which the science and art of medicine have conferred upon the human race; there is no moral calculus that can grasp and comprehend the sum of their beneficient operations. Ever since the first dawn of civilization and learning, through

> 'the dark backward, and abysm of time,'

they have been the true and constant friends of the suffering sons and daughters of men. Through their ministers and disciples, they have cheered the desponding; they have lightened the load of human sorrow; they have dispelled or diminished the gloom of the sick-chamber; they have plucked from the pillow of pain its thorns, and made the hard couch soft with the poppies of delicious rest; they have let in the light of joy upon dark and desolate dwellings; they have rekindled the lamp of hope in the bosom of despair; they have called back the radiance of the lustreless eye and the bloom of the fading cheek; they have sent new vigor through the failing limbs; and, finally, when exhausted in all their other resources, and baffled in their skill — handmaids of philosophy and religion — they have blunted the arrows of death, and rendered less rugged and precipitous the inevitable pathway to the tomb. In the circle of human duties, I do not know of any, short of heroic and perilous daring, or religious martyrdom and self-sacrifice, higher and nobler, than those of the physician. His daily round of labor is crowded with beneficence, and his nightly sleep is broken, that others may have better rest. His whole life is a blessed ministry of consolation and hope."

The last of Bartlett's strictly medical publications was a little monograph on the "History, Diagnosis and Treatment of Edematous Laryngitis," published in Louisville at the time he held the chair of practice at the University, in 1850. It is a carefully prepared monograph, based largely on the studies of Valleix, and to which a fresh interest had been given him by the observations of Dr Gurdon Buck, of New York, who

had cured several cases by directly scarifying the edematous membranes.

IV.

Naturally studious, fond of poetry, history, biography and literature in general, and not for long tied and bound in the chains of general practice, Bartlett had ample opportunities to cultivate his mind. He says in one of his letters to Green (dated Pittsfield, Nov. 1, 1835): "I pass a good deal of my time here quite alone, so that I find myself whiling away the hours in meditation much oftener than when engaged in the more varied and active affairs of business at home. I think that I always leave Pittsfield with the better and purer part of my being somewhat strengthened." Burton concludes his immortal treatise with the advice: "Be not solitary, be not idle," but the true student in some part of his life at least, should know the "fruitful hours of still increase." For many years Bartlett enjoyed a leisure known to-day to few professors of medicine, the fruits of which are manifest in his writings. Among his contemporaries in the profession there were brilliant writers, — Samuel Henry Dickson, Jacob Bigelow, J K Mitchell, — but in a style so uniformly high and polished, yet withal so plain, not one of them approached Bartlett. Compare, for example, Samuel Jackson's "Principles of Medicine," written in 1832, with the first edition of the "Fevers" (1842) — the one pompous, involved, obscure; the other clear, direct, simple. For style in his medical writings Bartlett may be called the Watson or the Trosseau of America.

Bartlett was at his best in the occasional address, and, as we have noticed already, this talent was cultivated very early in his career, since we find him giving the Fourth of July oration before his fellow-citizens when he had been scarcely a year in Lowell. All of the lectures and addresses illustrate, as Holmes said, "that easy flow of language, that facility of expression, that florid warmth when occasion offers, which commonly marks the prose of those who are born poets." Among these addresses there are four or five worthy of a permanent place in our literature. Perhaps the most characteristic is one entitled, "The Head and the Heart, or the Relative Importance of Intellectual and Moral Education," which is a stirring plea for a higher tone in social and political morality. In the same clear, ringing accent he speaks in his address on Spurzheim of the dangers of democracy. In a lecture on the "Sense of the Beautiful," delivered in 1843, Bartlett appears as an apostle of culture, pleading in glowing language for the education of this faculty. One short fragment I must quote: "Amongst the Hebrews, and in the age of Moses, it was linked to religion; it dwelt amidst the mysteries of Worship and Faith. It brought costly offerings to the costlier altar; it hung the tabernacle with its curtains of fine twined linen, and blue, and purple, and scarlet; and with cherubim of cunning work; it arrayed the high priest of Jehovah in his gorgeous and consecrated garments, and on the mitre of pure gold upon his forehead, it graved, like the engraving of a signet — Holiness to the Lord. At a later day, and amongst a widely different people, it became the handmaid of a refined and luxurious sensuality. It lapped the soul of Greece in a sensual elysium. Its living impersonations were Pericles and Aspasia. It called the mother of love from the froth of the sea, and bound her zone with its cestus; it filled the hills of Arcady with fleet Oreads; it graced with half naked Naiads the fountains and the rivers. It crowned the Acropolis with the Parthenon, and it embodied its highest conceptions of physical grace and beauty in the Venus and the Apollo. At other periods during the history of our race, it has manifested itself in other forms than these; under other circumstances, aspects and influences, and with other results."

In 1848 he delivered the Fourth of July oration before his old friends in Lowell. At the opening he refers to the fact that twenty years before he had occupied the same position. "It was the dewy morning of my manhood; 'time had not thinned my flowing hair'; life, with its boundless hopes and its golden visions, spread far and fair before me; and cheered by your words of encouragement, and aided by your helping hands, — your associate and co-worker, and in your service; a stranger, but welcomed with frank confidence and trust, — I had just entered upon its arduous and upward pathway."

In 1849 appeared a "Brief Sketch of the Life, Character and Writings of William Charles Wells," the South Carolinian Tory, who subsequently became a distinguished man of science in London, and who was well known for his researches on the phenomena of dew.

One of the last of Bartlett's publications was "A Discourse on the Times, Character and Writings of Hippocrates," delivered as an introductory address before the trustees, faculty and medical class of the College of Physicians and Surgeons, at the opening of the session of 1852-53. The three pictures which he gives of Hippocrates, as a young practitioner in the Isle of

Thasos, at the death-bed of Pericles, and as a teacher in the Isle of Cos, are masterpieces worthy of Walter Savage Landor, and I regret that time does not permit me to make quotations. In no words of exaggeration the late George D Prentice said, "There are but few word pictures in the English language that exceed the grandeur and loveliness of that one called into being by Dr Bartlett in which he imagines Pericles upon his death-bed with Hippocrates in attendance."

It is remarkable how many physicians write poetry, or what passes as such. I have been told of a period in the history of the Royal College of Physicians of London when every elect (censor), as they were called, had written verses. Some begin young, as did Bartlett; others become attuned in the deep autumnal tone of advancing years, when, as Plato tells us in the *Phaedo*, even Socrates felt a divine impulsion to make verses before quitting the prison house. Those of us who have read the epic of the late distinguished Professor George B Wood, of the University of Pennsylvania, entitled, "First and Last," published when he was sixty-four, will devoutly hope that professors of medicine, when afflicted with this form of madness, will follow his example and publish their poems anonymously and in another country. Jacob Bigelow, too, when nearly seventy, "darkened sanctities with song" with his American "Rejected Addresses" (Eolopoesis).

Dr Bartlett had poetical aspirations early in life. In a letter to his sister of December 3, 1826, he speaks of having seen in New York, in the *Garland,* "two fugitive pieces which some months before I had made use of to fill up the corner of a newspaper, but what sense they might have contained had been turned into nonsense, and I blushed for my wandering orphans, notwithstanding they had been so well dressed, and though they had found their way into pretty respectable company. I should have blushed for myself had they been exhibited to the public as my offspring." In another letter of the same period we see how completely he had passed beneath the yoke of Byron.

At the end of December, 1854, Bartlett issued a little volume entitled, "Simple Settings in Verse, for Six Portraits and Pictures from Mr Dickens's Gallery," the inditing of which had been, as he says, a pleasant occupation which had helped to while away and fill up many an hour which would otherwise have been weary or vacant in his invalid life. I have already spoken of one, "An Allegory," in which are autobiographical details. I cannot do better than to quote from an appreciative notice which his friend Oliver Wendell Holmes wrote of the little volume. "When, to the friends he had loved, there came a farewell gift, not a last effort of the learning and wisdom they had been taught to expect from him, but a little book with a few songs in it, songs with his whole warm heart in them, they knew that his hour was come, and their tears fell fast as they read the loving thoughts that he had clothed in words of natural beauty and melody. The cluster of evening primroses had opened and the night was close at hand."

Of a warm, affectionate nature, — a manhood fused with female grace, — to judge from the statements of contemporaries and friends, to know Bartlett was to love him. His confrères, John Orne Green and Alonzo Clark, are invariably addressed as "Dear Brother." Among the letters is one of sympathy to Dr Green, the desire of whose eyes had been taken away at a stroke. In it Bartlett unlocked his heart in a most touching and human appeal to the afflicted soul. It seems almost too sacred to quote, but after listening you will forgive me:

My Dear Brother: What shall I say to the melancholy allusion, in the close of your letter, to the death of our dear Minerva? What poor words of mine can be of any service to one on whom the hand of the Great Chastener has been so heavily laid? How shall I, whose life has been comparatively so cloudless and serene, come, with the message of solace and encouragement, into the presence of one whose meridian sun has been shrouded in such utter and dreadful eclipse? But why should I not? Am I not a brother and a man? Has not bereavement been a guest in the dwelling of my childhood; has not death been a familiar visitor amid the scenes of my early friendships and happiness and hopes? And where, too, is the future — for us all — for me, as well as for yourself? We but follow each other through the furnace of affliction, as we follow each other to the grave. Who of us had so hedged in his earthly treasures that the spoiler cannot easily break through the frail enclosure, and rifle him, in a moment, of the choicest and best? The lines of the Christian poet, familiar to me, chiefly, from the lips of a now sainted mother, occur to my memory here:

> 'The spider's most attenuated thread
> Is cord, is cable, to man's tender tie
> On earthly bliss; — it breaks at every breeze.'

We are brothers, then, in all the liabilities and contingencies and uncertainties of the future. Let us be brothers and fellow-helpers, also, in its

hopes and its duties. There can be no entire and hopeless wretchedness for the soul of man, except that which arises from its self-inflicted degradation. The sweet sister, the affectionate daughter, the beautiful bride, and the young mother, was taken away in the clear, unclouded morning of her life — taken away, but where? And by whom? The flower was transplanted from an earthly garden — a fair and sunny one, it is true, but from an earthly garden — to be set forever where no worm can feed on its root, where no decay can ever dry up its bloom — in the Paradise of God. By whom? Taken away — by her Father, from a far-off country, where she was only a sojourner or a pilgrim — to her beautiful and eternal home. Take these thoughts into your heart, and they shall lighten up, or drive away, the darkness of the past, and, what is better, they shall again cheer your future with the once familiar forms and faces of Happiness and Hope. How can we know what, even of present good, our indulgent Father may have in store for us? He may have allotted to you many long years, to be filled up first with duty, and, if filled with duty, to be crowned, also, with the cheerful light of social and domestic joy. You may say, perhaps, that this is all very well for me to say, but that I know nothing about it. But I do know something of the mutability of all earthly things. This uncertainty has long been to me a daily theme of meditation; so I am not wholly a stranger. But I have found an antidote to the gloom and sadness which would otherwise occasion in remembering that all things are in the hands of a Wise Disposer, and the surest way to please Him, as well as to secure our own present as well as future peace, is to submit to His dispensations and to follow on in the course of active and cheerful duty to Him, to our fellows and to ourselves."

While at Louisville some obscure nervous trouble, the nature of which I have not been able to ascertain, attacked Dr Bartlett. Against it in New York he fought bravely but in vain, and after the session of 1853-54 retired to Smithfield, his native place. The prolonged illness terminated in paralysis, but, fortunately, did not impair his mental faculties in the slightest. He died on the 19th of July, 1855.

From the many eulogies which appeared after Bartlett's death, I select a portion of one written by his dearest friend, Alonzo Clark, as the preface to the fourth edition of the "Fevers." "Sixteen months ago, he closed his brilliant professional career, after years of growing bodily weakness and pain; his mind not dimmed by his physical infirmities, but bright and comprehensive, glowing with the memories of the past, and the visions of the future. He died too soon for the profession he adorned. The clock had hardly marked twelve at noon, on the dial plate of life, when its pendulum strokes grew faint and gradually fainter to the ear; and now, at length, when all is still, the hand that notes the hours points sadly upward, to indicate how much of daytime still remained to reap the harvest of affection and honor in those fields from which he had already garnered up so many golden sheaves. He died, alas! too soon. The whole profession are his mourners; for conspicuous as he had become by his medical writings and his extended professional labors, his acknowledged worthiness, his innate gentleness and modesty disarmed envy. He left no enemies. His mind and purpose were pure, almost beyond example. His high mental endowments were controlled and directed by a considerate judgment and an earnest, benevolent heart; and as the laws of refraction, wrought out into mathematical formulae, enable the lapidary to construct the facets which open the fountains of the many-colored diamond, so, for him, cultivation and elegant taste had brought out the varied and winning native lights of his rich, intellectual, moral and social nature."

In translating the "Lives of Eminent French Physicians," Bartlett said he had a two-fold object: "First, the delineation of distinguished professional character and attainment, and, secondly, by the influence of such high examples to awaken in the younger members of the medical body a more devoted and worthy emulation of the great masters of our art." In this spirit I appear before you to-day, glad to tell over the story of your countryman — the story of "a life in civic action warm," one that all "the muses deck't with gifts of grace," a distinguished teacher, an author of widespread influence and distinction, a serene philosopher, but above all a man in whom you may recognize, even from the brief and imperfect sketch which I have given,

"A likeness to the wise below,
A kinship with the great of old."

Footnotes

[1] Parsons closes his Historical Tract on the Brown University Medical School with the sentence, "Whether this city, the second in New England, shall become the seat of such a school (that is, a revived department of medicine) must depend very much on the zeal, persistence and ability of its physicians." May I be permitted to remark, Mr. President, that the existing conditions are singularly favorable for a small first-class school. Here are college laboratories of physics, chemistry and biology, and modern hospitals, with three hundred beds. What is lacking? Neither zeal, persistence nor ability on the part of the physicians, but a generous donation to the University of a million dollars with which to equip and endow laboratories of anatomy, physiology, pathology and hygiene. These alone are lacking; the preliminary scientific school is here; the clinical school is at your doors; the money should be the least difficult thing to get in this plutocratic town. The day has come for small medical schools in university towns with good clinical facilities.

[2] Morse's Life, vol. i., p. 109.

[3] History of the Medical Department of Transylvania University and its Faculty, by William J. Calvert, Johns Hopkins Hospital Bulletin, August, September, 1899.

[4] Influence of Louis on American Medicine, Johns Hopkins Hospital Bulletin, August, September, 1897.

[5] Gross; American Medical Biography, 1861, p. 750.

A TIP FOR TEEN

STRESS

It's not easy being a teenager . . . Exercise can relieve some of the tension and improve your fitness. Exercise with a friend. You can talk about what's bugging you while you help each other get through your workout.

For more information, write to: Fitness, Dept. 84, Washington, DC 20001.

The President's Council on Physical Fitness and Sports

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

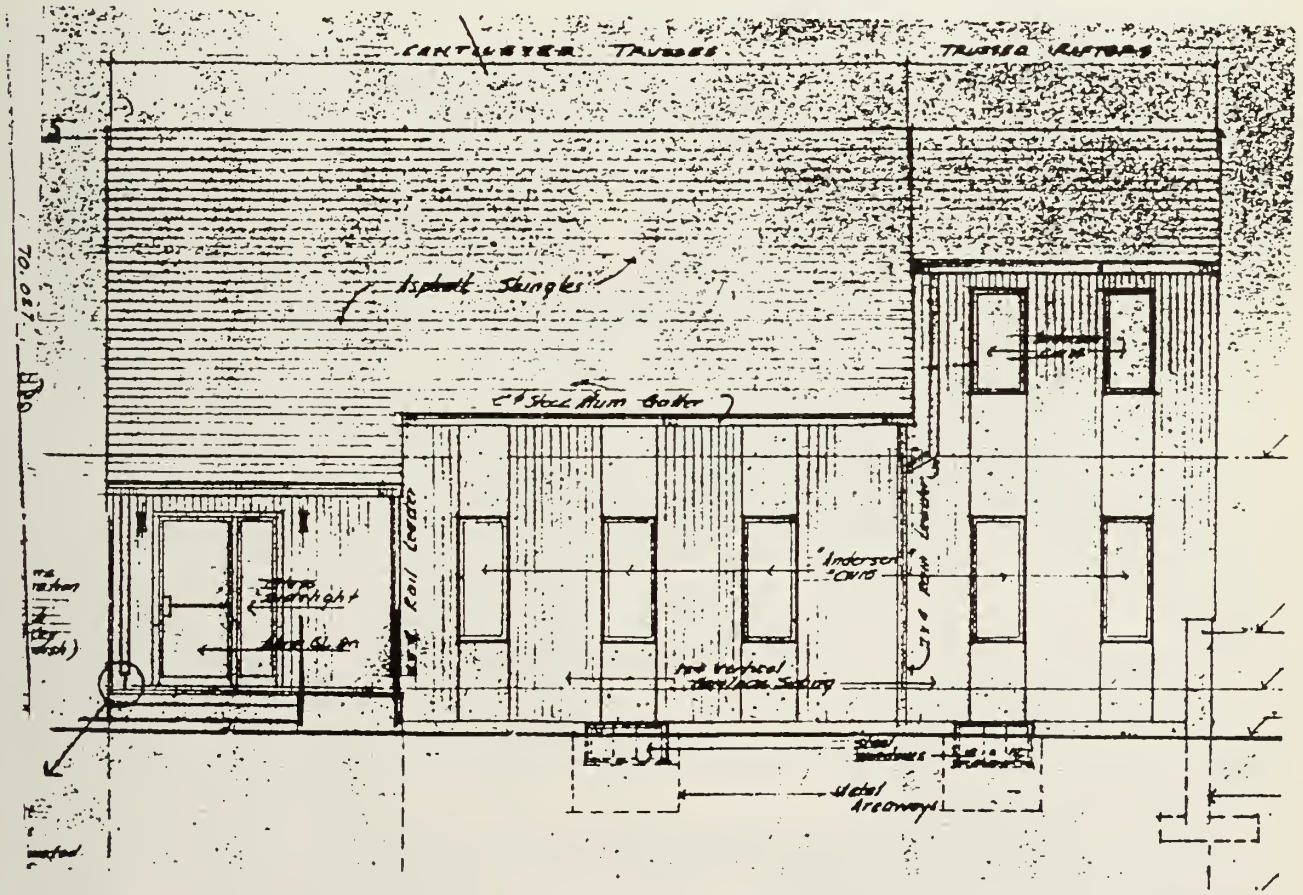
It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

FOR SALE OR LEASE

LINCOLN
PROFESSIONAL OFFICE BUILDING! ! !

TWO FLOORS
(NEW CONSTRUCTION)
PLANS AVAILABLE
2300 SQ. FEET

* REST ROOMS * FIRE ALARM * CENTRAL AIR CONDITIONING
* VAULTED CEILINGS WITH BALCONY * HANDICAP ACCESSIBILITY



* AMPLE PARKING * EXCELLENT LOCATION * QUALITY WORKMANSHIP

CALL
Michael Carolla
at
J. W. RIKER
725-8880

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

MEDICAL SUITE AVAILABLE FOR RENT

1240 square feet
ample parking

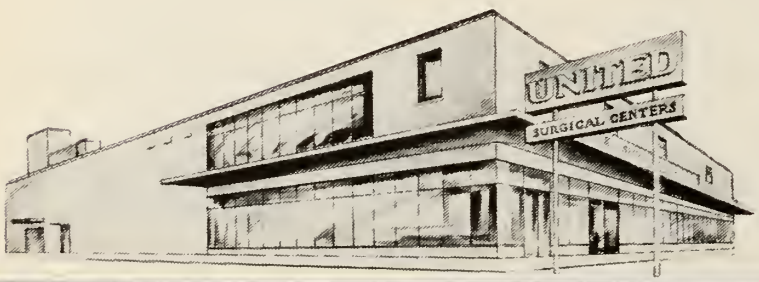
Barrington Medical Center
East Providence

Call 433-2400

There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

Motrin® 800 mg TABLETS
ibuprofen

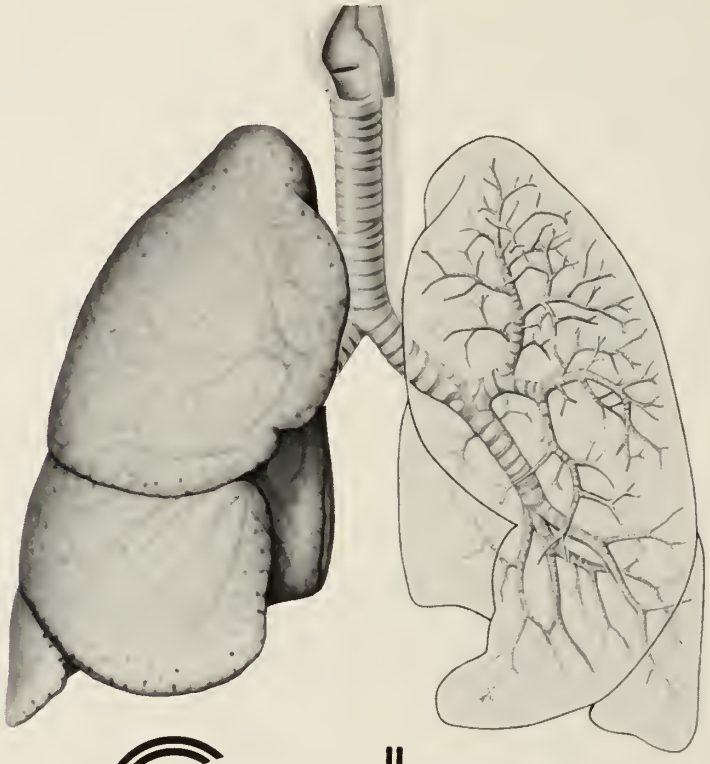
Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae, Streptococcus pneumoniae
(ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indications: Lower respiratory infections, including pneumonia, caused by susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae,* and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Contraindication:
Known allergy to cephalosporins.

Warnings:
CECLOR SHOULD BE ADMINISTERED CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. PENICILLINS AND CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY. POSSIBLE REACTIONS INCLUDE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly).

{072886R}

PA 8794 AMP

©1987, ELI LILLY AND COMPANY

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

700241

Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ:L42

In Hypertension*... When You Need to Conserve K^+

Remember the Unique Red and White Capsule: Your Assurance of SK&F Quality

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions)

Potassium-Sparing

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Over 20 Years of Confidence

The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

a product of

SK&F CO.

Carolina, P R 00630

© SK&F Co., 1983

There's never been a better time for her...

and PREMARIN®

Proven benefits beyond relief of vasomotor symptoms

No other estrogen proven effective for osteoporosis

Only conjugated estrogens tablets have established efficacy in both osteoporosis[1] and vasomotor symptoms* at 0.625 mg/day. No other estrogen, oral or transdermal, has established clinical evidence or minimum effective dose in both indications.

No estrogen proven safer

PREMARIN is the most extensively tested estrogen, with an unsurpassed record of long-term safety.
And clinical evidence shows a significantly reduced risk of endometrial hyperplasia when cycled with a progestin.[2]

PREMARIN®
(conjugated estrogens tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms.

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms and for osteoporosis

PREMARIN®
(conjugated estrogens tablets)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(conjugated estrogens)

Vaginal Cream

0.625 mg/g

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULARS)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream, in a nontiquefying base

1 ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA
Three independent, case-controlled studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year This risk was independent of the other known risk factors for endometrial cancer These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade The three case-controlled studies reported that the risk of endometrial cancer in estrogen users was about 4 5 to 13 9 times greater than in nonusers The risk appears to depend on both duration of treatment and on estrogen dose In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible When prolonged treatment is medically indicated, the patient should be reassessed on at least a semi-annual basis to determine the need for continued therapy Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration, it therefore appears prudent to utilize such a regimen Close clinical surveillance of all women taking estrogens is important In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding adequate diagnostic measures should be undertaken to rule out malignancy There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equi-estrogenic doses
2 ESTROGENS SHOULD NOT BE USED DURING PREGNANCY
The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring It has been shown that females exposed in utero to diethylstilbestrol, a nonsteroidal estrogen, have an increased risk of developing, in later life, a form of vaginal or cervical cancer that is ordinarily extremely rare This risk has been estimated as not greater than 4 per 1,000 exposures Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix Although these changes are histologically benign, it is not known whether they are precursors of malignancy Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb-reduction defects One case-controlled study estimated a 4 7-fold increased risk of limb-reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion) Some of these exposures were very short and involved only a few days of treatment The data suggest that the risk of limb-reduction defects in exposed fetuses is somewhat less than 1 per 1,000 In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well-controlled studies that progestogens are effective for these uses If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters Tablets are available in 0 3 mg, 0 625 mg, 0 9 mg, 1 25 mg, and 2 5 mg strengths of conjugated estrogens Cream is available as 0 625 mg conjugated estrogens per gram

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP) Moderate-to-severe *vasomotor* symptoms associated with the menopause (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) Osteoporosis (abnormally low bone mass) Atrophic vaginitis Kraurosis vulvae Female castration

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae

PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING)

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes Whether this will provide protection from endometrial carcinoma has not been clearly established There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens (See PRECAUTIONS.) The choice of progestin and dosage may be important, product labeling should be reviewed to minimize possible adverse effects

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions
1 Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease 2 Known or suspected estrogen-dependent neoplasia 3 Known or suspected pregnancy (see Boxed Warning) 4 Undiagnosed abnormal genital bleeding 5 Active thrombophlebitis or thromboembolic disorders 6 A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy)

WARNINGS: Estrogens have been reported to increase the risk of endometrial carcinoma (see Boxed Warning) However, a recent large, case-controlled study indicated no increase in risk of breast cancer in postmenopausal women A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement, it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use They should be used with caution in patients with cerebral vascular or coronary artery disease Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism, and thrombophlebitis When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives For this reason, diabetic patients should be carefully observed Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed Conditions influenced by fluid retention, such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients Oral contraceptives appear to be associated with an increased incidence of mental depression Patients with a history of depression should be carefully observed Pre-existing uterine leiomyomata may increase in size during estrogen use The pathologist should be advised of estrogen therapy when relevant specimens are submitted If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not yet complete If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism

The following changes may be expected with larger doses of estrogen
a Increased sulfobromophthalein retention.
b Increased prothrombin and factors VII, VIII, IX, and X, decreased antithrombin 3, increased norepinephrine-induced platelet aggregability
c Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T_4 by column, or T_4 by radioimmunoassay Free T_3 resin uptake is decreased, reflecting the elevated TBG, free T_4 concentration is unaltered
d Impaired glucose tolerance
e Decreased pregnanediol excretion
f Reduced response to metyrapone test
g Reduced serum folate concentration
h Increased serum triglyceride and phospholipid concentration

As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk

Long-term, continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver However, in a recent, large case-controlled study of postmenopausal women there was no increase in risk of breast cancer with use of conjugated estrogens

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives breakthrough bleeding, spotting, change in menstrual flow, dysmenorrhea, premenstrual-like syndrome, amenorrhea during and after treatment, increase in size of uterine fibromyomata, vaginal candidiasis, change in cervical erosion and in degree of cervical secretion, cystitis-like syndrome, tenderness, enlargement, secretion (of breasts), nausea, vomiting, abdominal cramps, bloating, cholestatic jaundice, chloasma or melasma which may persist when drug is discontinued, erythema multiforme, erythema nodosum, hemorrhagic eruption, loss of scalp hair, hirsutism, steepening of corneal curvature, intolerance to contact lenses, headache, migraine, dizziness, mental depression, chorea, increase or decrease in weight, reduced carbohydrate tolerance, aggravation of porphyria, edema, changes in libido

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1 *Given cyclically for short-term use only* For treatment of moderate-to-severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0 3 mg to 1 25 mg or more daily) The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible Administration should be cyclic (eg, three weeks on and one week off) Attempts to discontinue or taper medication should be made at three- to six-month intervals

2 *Given cyclically* Osteoporosis Female castration Osteoporosis —0.625 mg daily Administration should be cyclic (eg, three weeks on and one week off) Female castration—1 25 mg daily, cyclically Adjust upward or downward according to response of the patient For maintenance, adjust dosage to lowest level that will provide effective control

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only For treatment of atrophic vaginitis or kraurosis vulvae

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible
Administration should be cyclic (eg, three weeks on and one week off)
Attempts to discontinue or taper medication should be made at three- to six-month intervals
Usual dosage range 2 g to 4 g daily, intravaginally, depending on the severity of the condition
Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding

References:

1. Lindsay R, Hart DM, Clark DM The minimum effective dose of estrogen for prevention of postmenopausal bone loss *Obstet Gynecol* 1984,63 759-763 **2.** Studd JWW, Thom MH, Paterson MEL, et al The prevention and treatment of endometrial pathology in postmenopausal women receiving exogenous estrogens, in Pasetto N, Paoletti R, Ambrus JL (eds) *The Menopause and Postmenopause* Lancaster, England, MTP Press Ltd, 1980, chap 13

© 1987 Ayerst Laboratories
All rights reserved

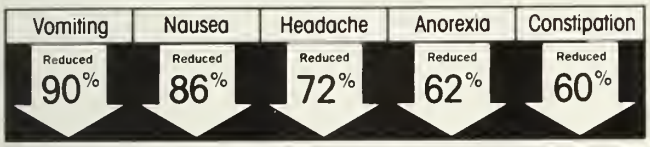
6437/587

Ayerst AYERST LABORATORIES
New York, NY 10017

See the difference in the first week[1]

- **Sleep improvement in 74% of patients after first h.s. dose[2]**
- **Significantly faster relief–62% of total four-week improvement evident in first week versus 44% with amitriptyline alone[1]**
- **Dramatic first-week reduction in somatic complaints[2]**

% Reduction in Somatic Symptoms[2]



- **Only ⅓ the dropout rate due to side effects of amitriptyline alone, although the incidence of side effects is similar[1]**

Caution patients about the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to the lowest effective amount in elderly patients.

Protect your decision.
Write "Do not substitute."

In moderate depression and anxiety

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) (IV)

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) (IV)

Copyright ©1987 by Roche Products Inc. All rights reserved.

References: 1. Feighner JP, *et al. Psychopharmacology 61* 217-225, Mar 22, 1979 **2.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ

Limbitrol® (IV)
Tranquilizer—Antidepressant
Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of moderate to severe depression associated with moderate to severe anxiety
Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.
Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage. Withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).
Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.
Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.
The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:
Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.
Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.
Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.
Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.
Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.
Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.
Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.
Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.
Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.
Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.
Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly. Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.
How Supplied: *Double strength (DS) Tablets,* white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt); and *Tablets,* blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500, Tel-E-Dose® packages of 100, Prescription Paks of 50.

ROCHE®
ROCHE PRODUCTS INC
Manati, Puerto Rico 00701

PI 0585

The rewards of Limbitr
You're both smiling agai

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

See the difference in the first week[1]

In depressed and anxious patients, you can see the difference sooner—62% of total four-week improvement achieved in the first week with Limbitrol versus 44% with amitriptyline.[1]

In moderate depression and anxiety

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) (IV)

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) (IV)

ROCHE®

Please see summary of product information on adjacent page.

Rhode Island Medical Journal

November 1987
Volume 70, Number 11

DISPLAY SHELVES

CPR:
Is there adequate training in Rhode Island?
(See page 487)

CONTRIBUTIONS

487 CPR: Ready or Not? A Rhode Island Perspective

495 How to Write a Medical-Legal Report for Litigation with Insanity as the Defense

501 Acute Renal Failure With Anuria Caused by Aortic Thrombosis and Bilateral Renal Artery Occlusion. A Report of Two Cases

483 EDITORIAL

483 INFORMATION FOR AUTHORS

505 PERIPATETICS

509 HAVE YOU HEARD?

511 BOOKS RECEIVED

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

NOV 23 1987

AIM HIGH

A SPECIAL PRACTICE FOR SPECIALISTS

★

If you're a **Surgeon** or **OB/GYN** or **Other Medical Specialist,** the Air Force may have a special practice for you.

What makes it special? You'll enjoy an excellent pay and benefits package. There'll be more time to spend with your family. You'll receive 30 days of vacation with pay each year. And you will work with modern equipment and some of the most highly trained professionals in the world, serving your country and your patients. Now that's special!

Find out just how special your practice can be. Call

1-800-423-USAF

AIR FORCE

Motrin® 800 mg TABLETS
ibuprofen

Extra strength
Convenience
Economy

Upjohn
A Century of Caring
1886·1986

©1986 The Upjohn Company

J-6138 January 1986

ZOVIRAX®
(acyclovir)
CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes, as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next page.

Prevent recurrences month after month*

ZOVIRAX® (acyclovir) CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psycho-social difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies, the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤ 10 ml/min/1.73/m^2.

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200" - Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709

Copr © 1986 Burroughs Wellcome Co. All rights reserved 86-ZOV-5

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml *(1 teaspoonful)* contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg *(warning: may be habit forming)*, alcohol, 3.5 percent; in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

Rhode Island Medical Journal

November 1987
Volume 70, Number 11

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

***Edward R. Feller, MD**
Chairman

***Stanley M. Aronson, MD**
Contributing Editor

***Maurice M. Albala, MD**

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

***John F. W. Gilman, MD**

***Edwin J. Henrie, MD**

***Toussaint A. Leclercq, MD**

Robert V. Lewis, MD

Robert Powel
Student

***Peter L. Mathieu, Jr., MD**

***P. Joseph Pesare, MD**

***Sumner Raphael, MD**

Henry T. Randall, MD

***Guy A. Settipane, MD**

***David T. Barrall, MD**
Resident

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

NOV 23 1987

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

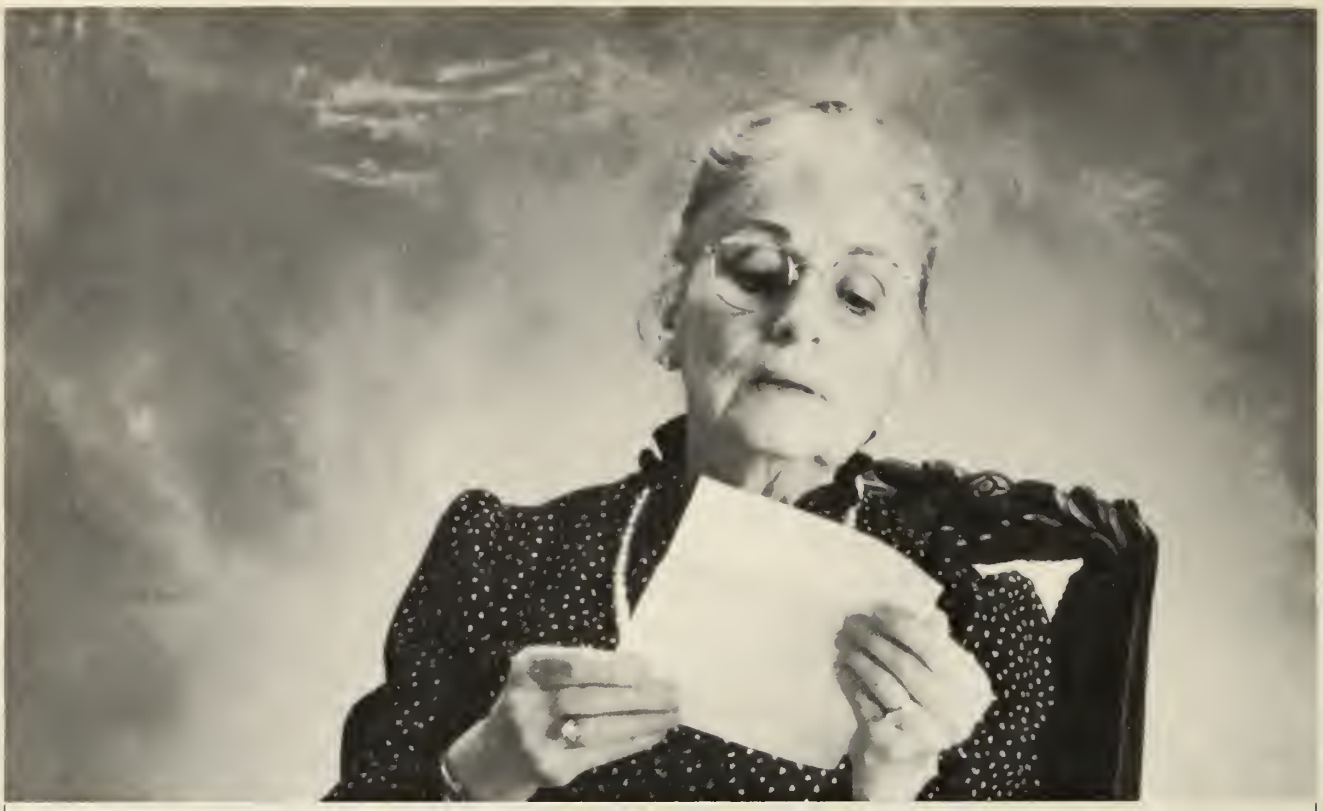
Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**



MARGARET WILSON RECEIVED HER DOCTOR'S BILL TODAY. AND SHE'LL PAY IT... JUST AS SOON AS SHE FIGURES IT OUT.

The problem is right in front of you. If your patients can't understand the statements you send them, they won't pay as quickly as you'd like. You'll probably receive a lot of unnecessary phone calls from confused patients demanding an explanation. And some patients may even decide to change doctors altogether. **P**erhaps *you* should make a change—to Contel Business Systems. We're the single-source solution to *all* your practice management problems. From patient accounting, automatic insurance billing, and electronic claims submission, to medical records, data base analysis, and word processing, our MENDS® II Practice Management System takes care of your business so you can take care of your patients. **A**t Contel®, we can provide the solutions to all your computer needs—including hardware and software selection, financing, installation, training, service, forms, and support. **A**nd, since we're part of Contel Corporation, a multi-billion dollar information services organization, we have the financial resources to serve you now, as well as in the future. **I**f you think your practice could benefit from our single-source expertise, call us toll-free at 1-800-4-CONTEL. Or fill out the coupon below. We'll help you explain the services you provide more clearly than ever before.
1-800-4-CONTEL

CONTEL® Business Systems

where business solutions begin

Contel Business Systems, Inc., One Dedham Place, Dedham, MA 02026-9990

Yes! I'd like to see my way clear to a more profitable future

☐ Please send me more information about Contel's MENDS II Medical Practice Management System

☐ Have a representative call me for a free needs analysis

Name _____

Title _____

Practice Name _____

Specialty _____

Address _____

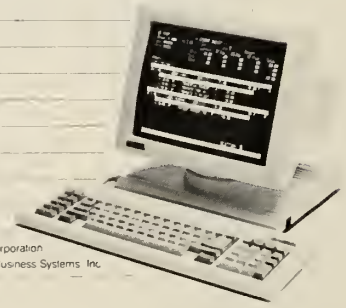
City _____

State/Zip _____

Telephone _____

Best time to call is _____

Contel is a registered trademark of Contel Corporation
MENDS is a registered trademark of Contel Business Systems, Inc.



Volume 70, Number 11 November 1987

TABLE OF CONTENTS

483 **EDITORIAL**

Poetic Justice

Seebert J. Goldowsky, MD

505 **PERIPATETICS**

509 **HAVE YOU HEARD?**

511 **BOOKS RECEIVED**

CONTRIBUTIONS

487 **CPR: Ready or Not? A Rhode Island Perspective**

More Trained Persons and Programs in Retraining Are Both Desirable

Jonathan Goldstein, MD
Augustine Manocchia, MD
Wayne Trotter, MD

495 **How to Write a Medical-Legal Report for Litigation with Insanity as the Defense**

Insanity Defense Is a Morality Play Starkly Contrasting Those Responsible and Those Not Responsible for Their Acts

Ronald Mark Stewart, MD
Thomas A. Jordan, MSW, LICSW
Susan Apshaga, BA

501 **Acute Renal Failure With Anuria Caused by Aortic Thrombosis and Bilateral Renal Artery Occlusion. A Report of Two Cases**

Atherosclerosis and a Superimposed Hypercoagulable State Frustrated Successful Treatment in Both Cases

Richard I. Fogel, MD
Raymond G. Endreny, MD
John J. Cronan, MD
Joseph A. Chazan, MD, FACP

COVER: *Photograph of CPR Training Program courtesy of American Red Cross, Greater Rhode Island Chapter, Providence, RI*

FOR SEVERE COUGHS, CAN YOU REMEMBER THESE LETTERS?

You know Robitussin®, and the "DAC" formula gives you just what you need to manage those severe coughs complicated with nasal congestion . . . Decongestant And Codeine!

Robitussin®-DAC℞

Each 5 ml (1 teaspoonful) contains:

Guaifenesin, USP	100 mg
Pseudoephedrine Hydrochloride, USP	30 mg
Codeine Phosphate, USP	10 mg

(Warning: May be habit forming)
Alcohol 1.4 percent

℞ ONLY

A·H·ROBINS
Pharmaceutical Division
Richmond, Virginia 23261-6609

EDITORIAL

Poetic Justice

On May 5, 1987 the First Annual Oppenheimer-Ginzburg Lecture on Inflammatory Bowel Disease was delivered at Mount Sinai Hospital in New York by Doctor Sidney Truelove, prominent British gastroenterologist. In 1932 a landmark paper appeared which described for the first time the entity of regional ileitis under the authorship of Burrill B. Crohn, Leon Ginzburg, and Gordon D. Oppenheimer. The endowed lectureship takes cognizance of the seminal contribution of the two junior authors, Oppenheimer and Ginzburg, who, while working in the surgical pathology laboratory of Mount Sinai Hospital, recognized the importance of a series of specimens submitted over a period of time by Doctor A. A. Berg, famed chief surgeon of the hospital. They described the pathological findings and correlated them with a new clinical entity. Doctor Crohn, a gastroenterologist, was a co-author of the paper. Being senior to the two young fellows in pathology, he placed his name first. From this historical accident, the disorder was given the designation (probably by British authors) of Crohn's disease, and it has been known as such ever since.

Most Mount Sinai buffs have long felt that it was gross injustice to the two men responsible for delineating this strange and difficult disease that it should bear the name of one who really was an incidental participant. At least so far as the hospital is concerned, this injustice has been somewhat mollified.

Doctor Truelove, formerly of the Radcliffe Infirmary of Oxford, is chairman of the International Organization for the Study of Inflammatory Bowel Disease. A pioneer in the treatment of this disease, he lectured on new analogues of sulfasalazine, which is a combination of a sulfonamide and aminosalicylic acid. The new drugs utilize the benefits of the aminosalicylic acid, while eliminating the side-effects of the sulfonamide.

It was poetic justice that Leon Ginzburg, himself a talented surgeon, and whole and hearty at age 89, was able to be present and enjoy the honor.

Seebert J. Goldowsky, MD

Information for Authors

Manuscripts: Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published or submitted elsewhere, and are submitted only to the *Rhode Island Medical Journal.*

Specifications: Manuscripts must be original typed copy (not all capitals) on 8½x11 inch firm typewriter paper, double-spaced (including the text, case reports, legends, tables, and references) with 1½ inch margins. Carbon copies will not be accepted. Subheadings must be inserted at reasonable intervals to break the typographic monotony of the text. Pages must be numbered consecutively. Italics and boldface print are never used except as subheadings.

Abbreviations: The *Journal* attempts to avoid the use of jargon and abbreviations. All abbreviations, especially of laboratory and diagnostic procedures, must be identified in the text.

Title page: All manuscripts must include a title page which details the following information: (1) a brief title; (2) the name of the author or authors with the highest academic degree (ie, MD, PhD); (3) a concise biographical description for each author which includes specialty, practice location, academic appointments, and primary hospital affiliation; (4) mailing address of principal author; and (5) office telephone number of principal author.

Illustrations: Authors are urged to use the services of professional illustrators and photographers. Drawings and charts should always be done in black ink on white paper. Clear, black and white glossy photographs should be submitted, and such illustrations numbered consecutively and their positions indicated in text. Original magnifications should be noted. Illustrations defaced by handwriting or excessive handling will not be accepted. The figure number, indication of the top, and the name of the author must be attached to the back of each illustration. Legends for illustrations should be typewritten in a single list, with the numbers corresponding to those on photographs and drawings. Recognizable photographs of patients are to be masked and must carry with them written permission for publication.

Special arrangements must be made with the editors for excessive illustrations. Color plates are not acceptable.

Reprints: Because of cost considerations, reprints are not provided routinely to the author(s). Reprints may be ordered separately (100 copies minimum order) and printing costs will be charged to the author(s).

Responsibility: Manuscripts are subject to editorial revisions as deemed necessary by the editors and such modifications as to bring them into conformity with *Journal* style. However, neither the editors, nor the publishers, nor the Rhode Island Medical Society will accept responsibility for statements made or opinions expressed by any contributor in any article or feature published in the pages of the *Journal.*

Permission: When material is reproduced from other sources, full credit must be given to both the author and publisher of these sources. Where work is reported from a governmental service or institution, clearance by the appropriate authority must accompany the manuscript.

References: References should be limited to those citations noted in the text. The references must be typed double-spaced and numbered as they appear consecutively in the text, with their positions clearly indicated in the text. All references must be checked to assure complete accuracy. Each journal reference must include the full name of the author(s); complete title of paper; name of publication; volume number; issue number; first and last page of paper; and date (year, month, and day as indicated). Each book reference must include the full name of author(s), editor(s), or both, with initials; title of book; edition; publisher; location; year of publication, volume (if given); and page number. If the reference is to a chapter within a book, the author of the chapter, if different than the author of the book, and the title of the chapter (if any) must be provided.

It is rarely desirable to include a complete review of the literature in the references. An alphabetized bibliography is to be used only when the listing is of books suggested for supplementary reading.

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:
- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE
OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue
Providence, R.I.
331-3996

120 Dudley Street
Providence, R.I.
331-3996

154 Waterman Street
Providence, R.I.
273-0450

38 Hamlet Avenue
Woonsocket, R.I.
766-4224

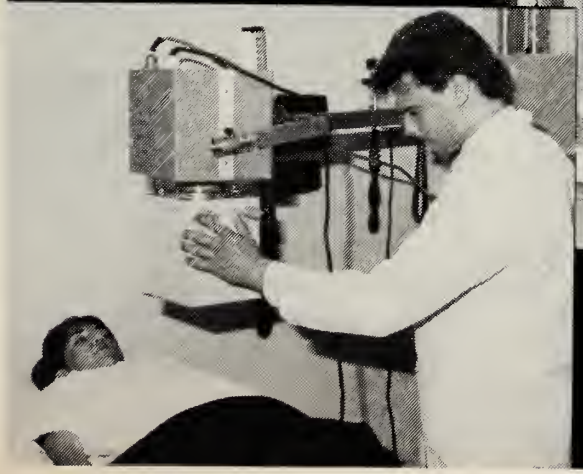
We've become the largest full service medical lab in Rhode Island... *because:*

- ✓ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✓ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✓ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✓ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

Statement of Ownership, Management and Circulation
(Required by 39 U.S.C. 3685)

1A. Title of Publication: *Rhode Island Medical Journal*
1B. Publication No.: 03637913

2. Date of Filing: September 30, 1987

3. Frequency of issue/Annual subscription price: Monthly/ $15.00

4. Location of known office of publication: 106 Francis Street, Providence County, Rhode Island 02903

5. Location of headquarters or general business offices of the publishers: 106 Francis Street, Providence, Rhode Island 02903

6. Names and addresses of publisher, editor, and managing editor:
Publisher: Rhode Island Medical Society, 106 Francis Street, Providence, RI 02903
Editor: Seebert J. Goldowsky, 106 Francis Street, Providence, RI 02903
Managing Editor: Kimberly J. Allyn, 106 Francis Street, Providence, RI 02903

7. Owner: Rhode Island Medical Society, 106 Francis Street, Providence, RI 02903

8. Known bondholders, mortgages, and other security holder owning 1 per cent or more of the total amount of bonds, mortgages or other securities: None

9. For completion by nonprofit organizations authorized to mail at special rates. The purpose, function, and nonprofit status of this organization and the exempt status for Federal income tax purposes has not changed during preceding 12 months

10. Extent and nature of circulation

	Average copies of issue during preceding 12 months	*Actual no. of copies published nearest to filing date*
A. Total no. of copies (Net press run)	1,769	1,775
B. Paid circulation		
1. Sales through dealers and carriers, street vendors, and counter sales	-0-	-0-
2. Mail subscription	1,659	1,683
C. Total paid circulation	1,659	1,683
D. Free distribution by mail, carrier or other means	8	8
E. Total distribution	1,667	1,691
F. Copies not distributed	102	84
G. Total	1,769	1,775

11. I certify that the statements made by me above are correct and complete.

Kimberly Allyn
Managing Editor

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY . . . . ANYWHERE

PLUS insurance for . . . .
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

CPR: Ready or Not? A Rhode Island Perspective

More Trained Persons and Programs in Retraining Are Both Desirable

Jonathan Goldstein, MD
Augustine Manocchia, MD
Wayne Trotter, MD

Since 1973, citizen-initiated cardiopulmonary resuscitation (CPR) has been established as a key first link in the community's emergency response team. For this scheme to work, some segment of the population must be taught CPR, and must be confident enough to use it and to use it with some degree of competency.

In this investigation, using a 12-item questionnaire, we attempted to determine exactly who has been instructed in CPR, retention of CPR performance knowledge, and general community attitudes toward CPR.

Jonathan Goldstein, MD is a second year resident in Neurology at Yale-New Haven Medical Center, New Haven, CT.

Augustine Manocchia, MD is a second year resident in Internal Medicine at Roger Williams Hospital, Providence, RI.

Wayne D. Trotter, MD is a second year resident in Internal Medicine at St. Vincent's Hospital, Worcester, MA.

Prepared in connection with the Community Health Clerkship, Brown University Program in Medicine, Providence, RI.

Our hypothesis was that the groups most able and best motivated to retain their CPR abilities would be: 1) younger aged, 2) well-educated, 3) related to individuals at high risk for sudden death, and 4) recently trained or having recently taken a refresher course.

Background

The present form of CPR has been used in an in-hospital setting since the early 1960s. The development of mouth-to-mouth ventilation preceded the 1961 report of Jude et al,[1] which described the effectiveness of circulatory support of a victim with an arrested heart with the prompt application of external chest compression. This was the birth of the modern era of resuscitation.

CPR or basic life support (BLS) are the terms applied to the proper utilization of these techniques of positive pressure ventilation and closed chest compression. Its purpose is maintenance of life until the victim recovers sufficiently to be transported to a hospital or until advanced cardiac life support (ACLS) is available. The technique attempts to center on the ABC steps of resuscitation — (a) airway, (b) breathing, (c) circulation — after proper recognition of cardiac and respiratory arrest.[2] CPR, therefore, is a temporary measure, which is the initial link in the emergency medical service chain.

CPR was taught in the 60s to firefighters and emergency medical personnel who would be the first professionals to respond to the scene of ac-

cidents and cardiac arrests. By 1971 the realization emerged that the first person on the scene of an arrest was virtually always an onlooker or citizen bystander, since surely the victim would not be calling rescue personnel. This led to the notion of training the citizen population in CPR, the belief being that survival chances of the victim might increase with earlier initiation of CPR.

This concept is based on the needs of the brain and other body tissues for oxygenated blood. Without such circulation for more than four minutes, irreversible anoxic cerebral injury will ensue. A minority of sudden coronary deaths (20-40 per cent) are due to myocardial infarction. The majority are due to dysrhythmias, especially ventricular fibrillation (VF), ventricular tachyrhythmias, and asystole, often secondary to underlying coronary artery disease. Sudden cardiac death occurs at an average of 300,000 times per year and is responsible for 75 per cent of all sudden non-traumatic deaths. A majority of these deaths are unexpected, in an out-of-hospital setting, and are the first presentation of coronary artery disease. A major obstacle to successful resuscitation of these individuals is a delay in initiation of resuscitation. Ventricular fibrillation can be corrected with a direct current countershock, but this requires the presence of an ACLS team to defibrillate electrically. This can be done rapidly in the hospital emergency room (ER) or coronary care unit (CCU) setting, but on the street a temporary measure is needed before personnel with equipment arrive. This is where initiation of CPR becomes crucial for delivery of oxygen, while the heart is unable to do so because of its electrical instability. A major determinant of outcome from a resuscitation effort is time between collapse and initiation of CPR, ideally less than four minutes, and between initiation of CPR to initiation of ACLS, ideally less than eight minutes.

In 1971 Cobb and Hallstrow[2] at the University of Washington in Seattle initiated a community CPR program (Medic II) to complement the firefighter (Medic I) emergency care system. Three-hour sessions were held stressing 1) recognition of cardiac arrest, 2) application of CPR (using mannequins for proficiency), 3) symptoms of heart attack, and 4) calling for assistance. The goal was to train citizens so they would be competent enough in CPR to administer it to the victim, without injuring the victim, until an emergency medical technician (EMT) arrived. In the Seattle experience the average response time from dispatch to arrival of Medic I was slightly less than three minutes. When life-threatening emergencies such as unconsciousness or symptoms of myocardial infarction were present, an acute life-support unit was also dispatched simultaneously. From data available in Seattle and nearby King County; Oslo, Norway; and Winipeg, Manitoba, survival (alive at discharge from hospital) with bystander CPR increased two-to five-fold in these urban and suburban communities with emergency care systems. The highest rates of survival were seen where ACLS was simultaneously dispatched to the scene.

Also noted in the Seattle experience was a decrease in the amount of neurologic sequelae in those who received rapid CPR application by a bystander at the scene. Sixty-one per cent regained consciousness in the first 24 hours following resuscitation, versus only 9 per cent of those not given early CPR. The incidence of prolonged coma and disorientation was also significantly reduced with application of bystander-initiated CPR. Another benefit of bystander CPR was decreased myocardial dysfunction as evidenced by a lower pulmonary capillary wedge pressure (PCWP) and a higher cardiac output (CO).

In Seattle in 1970-71 bystander-initiated CPR occurred in only 5 per cent of cases; by 1976 approximately 34 per cent of Seattle cases had CPR initiated by bystanders. In suburban King County 22 per cent were initiated by bystanders. In fact, out-of-hospital survival of arrest was greater than in-hospital survival of arrest, although an ambulatory arrest is more likely to be secondary to a primary rhythm disturbance, while hospital arrests are often secondary to or associated with advanced symptomatic illness. Such data make a strong case for lay CPR programs. By 1976 33 per cent of the Seattle population were trained in CPR, while in this country as a whole there is a steadily increasing number of long-term survivors annually (90-95) because of pre-hospital bystander CPR and emergency care.

A study in a paramedic-served area of Los Angeles (by Guzy *et al* at UCLA)[3] on bystander CPR and survival points up the strength of programs similar to Seattle's and why their results may not be duplicated elsewhere. Survival rates to discharge for all cardiac causes was 10 per cent, considerably less than the 23 per cent survival for all cardiac causes in King County and the 43 per cent survival for ventricular fibrillation (VF) in urban Seattle, which is also greater than the 27 per cent for the survival rate with CPR in Los Angeles. In this instance, although VF survival

rates were increased four-fold with CPR over the rate without CPR, they were unable to reach the levels seen in Seattle. The inability to measure up to Seattle can be attributed to one factor. The response time of the paramedics, which was in the range of 10-12 minutes, well beyond the critical eight minutes seen in the Seattle study. This points up the beneficial effects of the "tiered response" system in Seattle, in which the EMT or defibrillator can provide more rapid care prior to the arrival of a paramedic unit as used in Los Angeles.

In Rhode Island an emergency medical service (EMS) was formally organized in 1971 with training of EMTs with the goal of more definitive resuscitation and stabilization of victims in the field prior to transport to the trauma centers. Data from 1979 reveal that fewer than 8 per cent of patients with cardiac arrest treated by metropolitan Rhode Island rescue units were discharged alive from the hospital. This is indeed a far cry from the results in Seattle. A 1981 program to educate lay rescuers resulted in the training of approximately 6,000 individuals in Rhode Island, but still far from the 80,000 additional potential rescuers believed necessary to have a major impact on live discharge from the hospital.[4]

These two studies demonstrate some of the variables involved relative to how successful citizen CPR instruction can be in increasing survival. One of the largest problems related to CPR instruction is the ability of a potential rescuer to retain enough of his knowledge and psychomotor skills to be able to perform effective CPR. Several studies have been undertaken to determine skills retention of those trained in CPR.

In Seattle retesting was done on those who were trained in CPR six months previously. A decrease in performance level occurred, but when the same persons were retested at 12 months, their performance was better than those who had no interim reinforcement and were retested for the first time at 12 months. Their performance at 12 months was also worse than those who were initially tested at six months. The same trend was seen for those retested at two years, with a sharp decline in skills after two years. In another study by Fossel *et al* at Stanford,[5] significant differences were seen in performance between groups trained for longer than one year as compared to groups trained for longer than two years. They found that "the most frequent errors related to chest compression rate and inability to adhere to recommended single-rescuer compression-to-ventilation ratio." Rate-related errors accounted for 51 per cent of all failures. Technical errors, including inadequate compression, failure to release the compressed chest, and insufficent ventilation volume, accounted for 21 per cent of all failures. Both rate and errors in technique resulted in the remaining 23 per cent of failures. The single most common cause of failure was inability to achieve at least 50 compressions in a one minute period — 36 per cent of all those who failed did so solely on this basis.

Written examinations were given, but were not a reliable indicator of overall CPR performance. According to Fossel *et al*[5]: "In all but one instance though, if examinee could not identify the proper sequence of chest compressions to lung inflations (15:2) in single rescuer adult CPR on written examinations, he/she failed to perform adequate CPR. However, among those who gave the correct sequence on the examination, only 51 per cent performed adequate CPR."

Evaluation of skills retention by Wilson *et al* in Manitoba,[6] demonstrated maximum skills deterioration at 12 months, without further deterioration thereafter, but they were studied only at 14 months. They found that the most effective performance group on retesting were younger with the majority having had first-aid training in addition to CPR.

Another study by Bachman at the Mayo Clinic[7] found that skill loss is seen after both four-hour and eight-hour classes, although somewhat less after eight hours of classes.

From these types of study results, one might be encouraged if lay rescuers were younger, trained in first aid, and retrained every year with particular attention to motor skills and rates. Also, it would encourage four-hour classes in urban areas where a quicker EMS response should occur and eight hours of class in the suburbs where longer lay person CPR may be necessary before EMS personnel arrive.

There are, of course, other issues regarding who should be trained and relative to retention of skills and performance level. From the Seattle experience, data indicate that there is no difference in survival based on the quality of CPR performed. One could interpret from those survival results that the chest compressions were effective based on the increase in intrathoracic pressure, resulting in increased blood flow, rather than direct cardiac compression. Therefore, "bad CPR" may not be as useless as was thought in the past.

The Seattle investigators give four possible ex-

planations for the lack of difference in survival with varying levels of CPR performance. First, it is probable that the initiator of CPR is more likely to be better trained or more familiar and comfortable with the technique. Second, the rapid response of the fire department emergency team in the urban Seattle setting necessitated only a few minutes of bystander CPR. Survival may have decreased if the time needed to perform CPR was greater than 2-3 minutes. Third, survival may be too crude a measure of the quality of the CPR performed. Detailed neurologic study could be a better indicator of proficiency of CPR related to outcome. Finally, the CPR performed could really have been comparable regardless of occupation or training. There are important questions to answer, since it is unrealistic to expect near-perfect performances from persons who are unlikely to have the chance to perform more than once or twice in a lifetime.

Complications of CPR performed incorrectly include: vomiting with possible aspiration, gastric distention, fractures, and organ lacerations. In the study by Fossel,[5] there was an equal number of complications in groups as recently trained as 2-3 weeks, those at one year, and those at two years post-training. Also, 73 per cent of all otherwise adequate performances by these trained potential rescuers were marred by non-fatal complications.

Much has been written about who should be trained in CPR. Consideration has been given to those who have access to large public groups such as ushers, bus drivers, police, school teachers, and forest rangers. This strategy seems sound on a cost-benefit ratio, but there is no magic number of people to be trained to insure that a rescuer will be in the vicinity of a victim. Should everyone be trained? Based on reports of the Mayo Clinic,[7] the energy expenditure during 15 minutes of single-person CPR is equal to 5-10 minutes of treadmill exercise, a submaximum performance, but still enough to cause ischemic cardiac changes in a segment of the population.

A surprising result was obtained by Goldberg[8] at the University of Massachusetts in a study of CPR training in relatives of persons with coronary heart disease (CHD) or at high risk for sudden death. Their conclusion was that there was no significant difference in the proportion of family members of patients with CHD (22 per cent) who had taken CPR as compared to randomly selected controls. They also found that family members who had taken these courses had taken them further in the past than the control group. No mention is made of refresher courses in the study. The control group was also younger, which flaws the study. Of the 22 per cent who had taken a CPR course, only 9 per cent said it was related to their having family members at risk.

Five years after the initiation of the Seattle Medic II program, a survey was conducted to determine what type of person had been trained. They found that younger (average age 33 years), well-educated (past high school), white-collar workers were more likely to be trained. Also, 33 per cent of those who had been trained lived in a household with an individual over 50 years of age, while in Seattle 33 per cent of the entire population understood CPR. Are we targeting our CPR training efforts to the correct individuals?

Methods

The material of the study consisted of a random sample of 159 individuals with some period of residence in Rhode Island. Sampling was carried out in shopping centers in the cities of Warwick, Lincoln, and Providence. All participants were over the age of 14 and spoke English.

The method used for the study was a 12-question questionnaire which was orally administered by one of the investigators. One question — "Have you ever seen CPR performed?" — was not asked in all cases and was therefore stricken from further consideration.

Age, sex, and occupation were included to assess for possible bias in sampling. No bias was found in regard to sex or age. An attempt was made to avoid over-representation of any one profession or social class, such as those in the medical field. The significance of difference was calculated using the *chi*-square test with a standard *chi*-square table to determine probability values with one degree of freedom.

Results

1. *Do you know what CPR is?*

A correct answer to this question involved defining the process of performing CPR and the reason for doing it. There were 18 incorrect answers from the 159 Rhode Islanders surveyed. Thus, 11.3 per cent either defined CPR incorrectly or had never heard of it.

2. *Have you ever trained in CPR?*

An answer of "yes" to this question implied that that individual had fulfilled the requirements of instruction time of the American Red

Cross/American Heart Association for certification in CPR. From the standpoint of the general population studied, 40.3 per cent of Rhode Islanders surveyed had, in fact, trained in CPR. Considering that the standard CPR certificate is valid only until one year after the training period, we were interested in knowing whether or not those trained more than one year ago had taken a "refresher" course in CPR. Our data indicate that 45 persons trained in CPR had received a course more than one year before. Yet only 17 of these (37.8 per cent) had taken a "refresher" course in CPR. Of those 17 who had taken a refresher course, 12 (70.6 per cent) had done so less than two years ago.

As stated earlier in this paper, we were very interested in the importance of certain variables; ie age, level of education attained, presence/absence of a household member with cardiovascular disease of any kind, and desire to train in CPR. Age and level of education appear to be significant in propensity to train in CPR; while a diseased household member of the participant was not a factor.

When comparing age and propensity to learn CPR, we found that 47 of 100 persons in the less than 40-years-of-age category (47 per cent) had learned CPR. However, only 16 persons out of a sample of 57 people in the over-40 age category were so certified (28.1 per cent). The *chi* value for this analysis was 2 of 5.41, with a p value of .02.

When comparing the level of education with desire to become certified in CPR, we found that of the 76 participants who had had at least some high-school education, only 23 (30.3 per cent) had learned CPR. However, of the 63 participants with at least 2 years of college background, 29 (46.0 per cent) understood CPR; and 12 of the 17 participants with graduate degrees (or 70.6 per cent) had taken a course in CPR. Using the *chi*-square method, we analyzed the results comparing high-school and college education (disregarding the graduate school data due to the small sample size) and found a x^2 value of 3.66, with a p value less than 0.1.

When comparing the presence of a fellow household member with cardiovascular disease and propensity to train in CPR, we found that, of the 73 participants who admitted to having a household member with cardiovascular disease, 41 (56.2 per cent) had *not* trained in CPR. Of the 81 persons without diseased household members, 28 (34.6 per cent) had trained in CPR, while (as one can infer from the above) 43.8 per cent of those living with a person with cardiovascular disease had had training in CPR. The *chi*-square value for this study was $x^2 = 1.39$, giving a p value of 0.5. Cardiovascular disease in this study was defined as hypertension, angina, myocardial disease or valvular disease. Seventy-three of 154 responding participants (47.4 per cent) lived with a person with cardiovascular disease. Also, four of the respondents having a diseased family member were wives whose husbands had had coronary artery bypass graft surgery (CABG), yet none had trained in CPR.

3. Should everyone know how to perform CPR?

In studying the replies to this question, we explored the possibility that age and level of education might be factors in how the question was answered. By "everyone," we meant "the general population of Rhode Island." Out of the total 154 who responded to this question, 132 (85.7 per cent) agreed that everyone *should* know how to apply CPR.

When comparing age and responses to the question, we found that, of the 98 persons less than 40 years old, 94 (96 per cent) felt that everyone should understand CPR. However, of the 56 persons over 40 years of age, only 38 (67.9 per cent) had the same opinion. With a *chi*-square value x^2 of 22.92 the p value for this analysis was less than 0.001.

When comparing level of education and replies to the question, we found that, of the 80 respondents with at least some high-school education, 61 (76.3 per cent) were of the opinion that the entire general public should have knowledge of CPR. However, 55 of the 59 respondents with at least two years of college education (93.2 per cent) agreed, while 16 of 17 with a graduate degree (94.1 per cent) agreed on the importance of everyone knowing how to perform CPR. In comparing only high-school and college-educated respondents, the x^2 value was 7.08, with a p value less than 0.01. Those who responded negatively to the question in general felt that only physicians, nurses, and paramedics should have knowledge of CPR.

4. Could you perform CPR now if it were necessary?

In evaluating responses to this question, we found that, of the 64 respondents who had taken at least one course in CPR, 43 (67.1 per cent) believed that they could now perform CPR properly. We also compared the responses of those who had taken a refresher course less than two years before. All 12 of those who had taken a refresher course within two years answered in

the positive, while four of five who had taken a refresher course more than two years before answered in the positive ($x^2 = 2.60$, $p = 0.1$). We did not consider those who had taken a refresher course less than one year before because of the small sample size.

Only 17 of 64 respondents who had ever taken a course in CPR (26 per cent) correctly identified the proper ratio of compressions: ventilations during one-man CPR (15:2). Most of the responses were 15:1 or 5:1.

Discussion

CPR has a long history and has changed much over time. From the ventilatory support of the early period, CPR has progressed to active participation in maintenance of cardiovascular function. This has involved increasing participation by the residents of cities and suburbs in a potentially life-saving technique. Several groups have been targeted for intensive training in CPR as a means of increasing the availability of the skilled CPR providers. This consists mainly of lay persons as in the Seattle project.[2] In this paper we have focused on the current attitudes and training in such skills in Rhode Island, 25 years after the introduction in the state of the technique of CPR.

It is apparent that there are several significant trends in the Rhode Island population. The findings may help to explain the patterns of CPR use found in the lay community. The level of education was correlated with such attitudes as desire to train in CPR and who should be trained in CPR, with college-educated persons being more inclined to this view than high-school-educated individuals. This suggests that the areas more densely populated with trained persons might well be the same areas as those with a more highly educated population. This would create a problem for inner-city and rural populations where a resource such as CPR is invaluable. If this skewing of the availability of trainees does in reality exist, more intensive targeting to inner-city and rural populations must be undertaken. As to the correlation between age and training attitudes, it was found that persons under forty years of age had a greater desire to train in CPR and felt that everyone should be acquainted with CPR, persons over forty years of age held the opposite view. This is significant, since it is the older population which is at risk of sudden death and thus in need of resuscitation.

This becomes important when one considers that persons of the same age group tend to associate and thus are more likely to be in a position to utilize CPR. On the other hand, the younger persons are less likely to have need of CPR with their peers. This does not mean that young people should not be trained in CPR, but that the older population, such as the adult work force, retired persons, and nursing home residents should be targetted for training in CPR. In light of these findings, one can speculate that the younger population has been exposed increasingly to CPR techniques through education and media sources and thus may be more inclined to participate. This contrasts with the older population who may be confused or even skeptical about the use of this relatively new skill. Again, this reinforces the concept that the older populations should be educated in these methods. Finding the medium to accomplish this goal is a challenge for future years.

As to persons with family members having cardiovascular disease, there is no significant evidence that such persons have a greater incidence of training in CPR. The public appears not to associate the increased risk in their families with the need to be proficient in CPR. This represents another area where targeting of training and public education is needed. It is possible that persons with family members having cardiovascular disease have decreased health awareness and that the family as a whole is not interested in the benefits of risk reduction or, more specifically, CPR. However, these findings may signify lack of proper identification and education of subgroups who should know about CPR. In either case, this important information should generate new planning and organization of CPR training in Rhode Island.

The Seattle study[2] revealed that, while in 1971 only 5 per cent of CPR was initiated by bystanders, by 1976 34 per cent of CPR was so initiated. Thus, it is possible to create a program where large segments of the population can be trained in CPR. The importance of this training is emphasized when we find that only 8 per cent of cardiac arrest patients in Rhode Island treated by rescue were discharged alive.[4] The public must assume a larger role in implementation of emergency pre-hospital care in Rhode Island. Our study revealed that 12 per cent of the Rhode Islanders sampled did not know what CPR meant. This percentage should approach zero if public education programs are effective.

In view of these findings, it is apparent that the training in CPR in Rhode Island must be modified. It is not only the first-time training but

the continuing refreshers which create an effective CPR program. In Rhode Island only 26 per cent of the persons who had taken CPR courses correctly identified the proper compression-to-ventilation ratio. Further studies must be done regarding retraining methods and preventing decay of technical skills.

Our study indicated that many variables influence who and how many individuals are trained in CPR. These range from exposure to media coverage to health attitudes. In Rhode Island the end-effect is that the younger, more highly educated persons have an increased likelihood to be trained in CPR and have a feeling that the public should also have this training. The older population does not accord with this view. Determining the reason for this difference will be of great value in obtaining future participation of this group in emergency medical care.

Conclusions

There are several shortcomings in the present implementation of a community-based CPR program in Rhode Island. These include: 1) lack of involvement of the over-40 age group, 2) decreased participation by those less well educated, 3) lack of a proportional increase in CPR training among those having household members at increased risk of sudden death, and 4) poor compliance with American Heart Association recommendations regarding certification one year after training.

We propose several measures to overcome these deficiencies. We believe that older populations should be targeted for education regarding the value of CPR for themselves and their need for training. Emphasis should be placed on training those less well educated who comprise a group that has less access to CPR programs. We recommend that all physicians provide information on the value of CPR to all of their patients, especially those with family members at high risk of sudden death. Finally, we suggest that both the American Heart Association and the American Red Cross periodically implement large-scale media campaigns designed to encourage people to retrain.

References

[1] Cobb, L.A., Hallstrom, A.P. 1982 Community-based cardiopulmonary resuscitation: what have we learned? Ann NY Acad. Sci. 382:324-9.

ref. Jude J.R., Kouwenhouen, W.B., Knickerbocker, G.G. 1961. Cardiac arrest: Report of application of external cardiac massage on 118 patients. J. Am. Med. Assoc. 178:1063-70.

[2] Cobb, L.A., Hallstrom, A.P., Thompson, R.G. et al. 1980. Community Cardiopulmonary Resuscitation. Ann. Rev. Med. 31:453-62.

[3] Guzy, P.M., Pearce, M.L., Greenfield, S. 1983. The Survival Benefit of Bystander Cardiopulmonary Resuscitation in a Paramedic Served Metropolitan Area. Am. J. of Public Health. Vol. 73, No. 7.

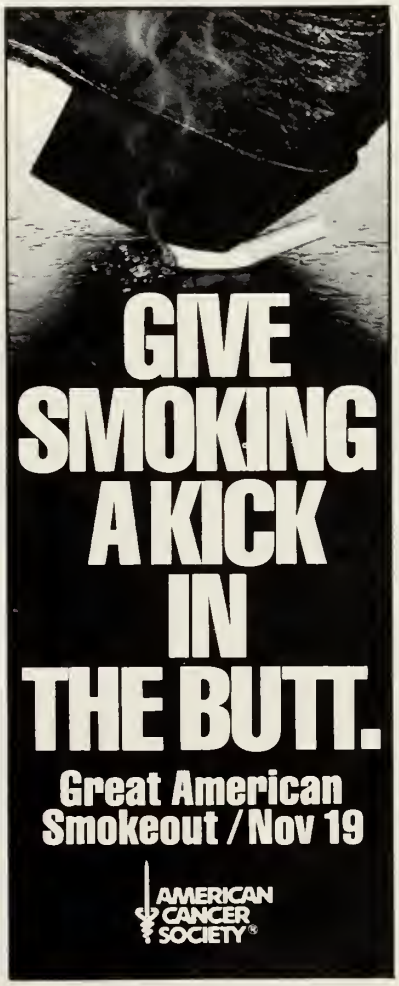
[4] Mitchell, G.W. 1982. Resuscitation in Rhode Island. R.I. Medical Journal Vol. 65:329-31.

[5] Fossel, M., Kiskaddon, R.T., Sternback, G.L. 1983. Retention of Cardio-Pulmonary Resuscitation Skills by Medical Students, J. of Medical Education Vol. 58:568-575.

[6] Wilson, E., Brooks, B., Tweed, W.A. 1983. CPR Skills Retention of Lay Basic Rescuers. Ann. of Emergency Medicine 12:482-484, August.

[7] Bachman, J.W. 1984. Cardiac Arrest in the Community: how to improve survival rates. Post Grad Med., Vol. 76/No. 3 September:85-95.

[8] Goldberg, R.J., Gore, J.M., et al. 1984. Layperson CPR — Are We Training the Right People? Ann. Emerg. Med. Part 1, 13:701-704.



You got the wrinkles ironed out of that investment property financing in no time. How'd you do it?

My Private Banker. Perrier?

Do you have substantial assets, or an income that's on the way up? A Hospital Trust Private Banker can provide maximum response to your investment and real estate financing needs. Your Private Banker has significant expertise for significant goals.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Perrier is a registered trademark of Great Waters of France, Inc.

Equal Opportunity Lender

How to Write a Medical-Legal Report for Litigation with Insanity as the Defense

Insanity Defense Is a Morality Play Starkly Contrasting Those Responsible and Those Not Responsible for Their Acts

Ronald Mark Stewart, MD
Thomas A. Jordan, MSW, LICSW
Susan Apshaga, BA

Psychiatrists, psychologists, and social workers frequently function as teams in a forensic setting. Together they possess the knowledge, skills, and criteria necessary to describe a defendant's mental condition, pathological beliefs, and motivations and to explain with particular regard to mental capacity and the crime charged how these factors influenced or could have influenced the defendant's behavior. They complete assessments of the patient within the framework of their specific disciplines and in conjunction with other medical professionals pertinent to the case.

Ronald Mark Stewart, MD, is Medical Director of Human Services Consultants LTD, Providence, RI, and Chief Psychiatric Consultant, Forensic Unit, Institute of Mental Health, Rhode Island Department of Mental Health Retardation and Hospitals, Cranston, RI.

Thomas A. Jordan, MSW, LICSW, is a Forensic Clinical Social Worker, Forensic Unit, Institute of Mental Health, Rhode Island Department of Mental Health Retardation and Hospitals, Cranston, RI.

Ms. Susan Apshaga, BA, is an MA candidate and freelance writer and editor.

It is then the task of the psychiatrist, the leader of the team, to synthesize the data for the purpose of understanding the difficulties experienced by the patient. However, depending upon circumstances, the social worker or psychologist may be designated to synthesize the data and write the consultation. Whoever ultimately is in this position, it is important that the evaluation be comprehensive.

The members of the team must be well versed in the language of the various disciplines. Each understands the others' reports as they are combined to influence the management and treatment of the patient. However, this mutual understanding does not always apply to non-medical participants, particularly members of the legal profession. The interface between psychiatry and law is complex, but the relationship need not be unsatisfactory on a day-to-day basis.

The purpose of this paper is to assist the clinician in completing a coherent medical-legal report of good quality. To that end, we shall focus upon the standardized approach to examination of a patient and recording the findings. The approach or format is somewhat flexible, subject to modification according to the practitioner's preference or the nature of the patient's problem.

A consultation report provided to an attorney is intended not primarily to influence treatment, but rather to describe and explain the patient's symptoms to the attorney, judge, or court. The

report thus supports either the patient's defense of lack of criminal responsibility; or the reverse, if appropriate. The report must be professionally objective.

Historical Overview

The insanity defense is at least 300 years older than the discipline of psychiatry and in modern form has led to a dominant role for the psychiatrist in the process. While there are issues relative to the scope and quality of psychiatric testimony, the literature offers no valid reasons for returning to previous centuries when experts were neither available nor necessary, when a jury decided on an intuitive basis whether or not a defendant appeared to be insane.[1]

The Report

I. Cover Letter. The cover letter should be addressed to the individual (judge, attorney, or other) who requested that the defendant be examined. Above the greeting, and at the far right of the first page, the defendant's name and birthdate should appear. If there is an active official case number, it should also appear.

The cover letter should state why the request was made: "to evaluate whether the defendant (or patient) can be held criminally responsible with regard to his/her current charges." The charge may be murder, first degree sexual assault, armed robbery, or other. The date that the alleged acts took place and where they occurred should also be stated.

The letter should state clearly that the purpose of the examination was explained to the patient, and that the patient had consented to the examination. It should be specified clearly that a patient either understood or did not understand that an examination was being conducted to determine if there was adequate data to proceed with a defense to the legal allegations against the patient or defendant of not guilty by reason of insanity.

The cover letter should conclude with a brief summary of what is contained in the medical-legal report.

II. Title. Each page of the report should be labeled "Medical-Legal Consultation: Private and Confidential," followed by the patient's name. Some practitioners prefer to label each page with the term: "Psychiatric Consultation." It is necessary that psychiatric consultations be clearly identified. The words "private and confidential" are meant to protect the patient and to prevent unauthorized persons from gaining possession of the report.

III. Identifying Data. The patient's name, age, sex, marital status, number of children, employment and address are listed in conformity with medical style. The practitioner can use these important demographic variables to present the patient as a person having all the relevant human relationships.

IV. The Examination. This section should state when and where the patient was examined and for what period of time. It should also list the sources for information obtained elsewhere, ie, previous medical records, social service records, and other relevant materials.

V. Conclusion Example. It could state: "In my opinion, the patient (state name) because of a mental disease or deficit lacked the capacity to appreciate the wrongfulness of his conduct to the requirements of the law." The wording would depend on the statutes governing such pleas in the given state. The form would be the same if, based on the psychiatric examination, it is concluded that there was an absence of mental disease or deficit and that the patient was capable of distinguishing right from wrong.

Supporting Information

To complete the initial part of the Medical-Legal Consultation the psychiatrist will have obtained all of the information available about a patient. The most relevant information is included in the consultation:

I. Personal History and Life Events. Any part of a person's personal history may be germane. It may contribute to the practitioners' efforts to understand the breadth and quality of a patient's interpersonal relationships, his level of adaptive functioning, and circumstances that may have had some impact on the patient's (or defendant's) behavior. Socio-cultural data should include birth, growth and development, current family interactions, financial situation, living arrangements, educational history, occupational history, and current work situation. Racial, ethnic, and religious differences are all considered when relevant.

II. Mental Status Examination. This is a clinical summary of the patient's thought process, thought content, mood and affect, and cognitive function. It can also include opinions as to whether a patient is diagnosed as being a danger to self or others.

The manner in which the mental status examination is communicated depends upon the referral source and the purpose for which it will be used. The discipline of psychiatry is involved in the defense or the prosecution of major criminal cases, or both. Either the prosecution, the defense, the court, or all three may request psychiatric evaluations on a defendant who utilizes insanity as a defense.

III. Discussion of Conclusion. Here the practitioner summarizes the patient's history to the extent necessary. The diagnosis of illness is stated, whether or not the illness is in remission, and if so, whether with or without the help of medications.

Discussion

Factors militating against the merit of the defense of "not guilty by reason of insanity" should be clearly presented. Those factors supporting the defense of insanity should also be clearly stated. Even though medical-legal reports should be as objective as possible, there are occasions when the psychiatrist is an advocate either for the defense or for the prosecution.

In our experience patients/defendants sometimes give different versions of events to psychiatrists or to attorneys. There is a great need to clarify the distortions and discrepancies. In changing his or her own assessments and conclusions, the psychiatrist must be ever cautious about yielding in situations that will make his/her expertise vulnerable in an adversarial system. The psychiatrist in the end must present a view of impartiality to the court. In this process, he or she can assist the attorney in making the best use of the information contained in the medical-legal consultation. We recommend that the consultation be honest and in the interest of justice and, even more, that it bridge the gap between treatment and justice if the case warrants it.

Clinicians are most certainly aware of the various societal viewpoints regarding psychiatric testimony. There are concerns among those professionals who must perform forensic assessments and render expert testimony. The lack of legal knowledge is a problem. Statutes relating to the insanity plea are sometimes vague. There is a hesitancy to get involved in the adversarial system. Such involvement can very well mean cross-examination by the attorney whose client the consultation does not favor. In such a setting the psychiatrist may also be confronted by a person of equal professional expertise who agrees with the facts, but offers an opposite interpretation.

These annoyances, however, do not diminish the need for professionals who offer testimony which assesses systematically the reliability and validity of psychiatric diagnoses. Nor do they nullify the importance of a thorough coherent consultation report based upon these diagnoses as a basis upon which the legitimacy of an insanity defense is determined. How attorneys use such testimony and consultation is another issue.

As far as the insanity defense itself is concerned, the authors concur with the opinions expressed by the National Commission on the Insanity Defense in its report titled *Myths and Realities.*[2] After conducting a national study, the Commission came to the firm conclusion that "the insanity defense, rooted in 500 years of history and religion, pruned and nurtured through the centuries by public officials, legal scholars, mental health experts, and society in general, should continue to be an integral part of our jurisprudence system."[2]

Summary

The National Commission on the Insanity Defense has described the process as "a morality play which brings into stark contrast those who are responsible and those who are not responsible for their acts." The expert testimony of psychiatrists and other therapists has made a direct contribution to the public conscience of the vital distinction between illness and evil. Expert testimony in such cases uses the written medical-legal report consultations as its foundation. The authors present a scheme for organizing the content of the medical-legal consultation.

Acknowledgements

The authors wish to thank Patricia Sullivan and Mary Ann Rossoni for their assistance in arranging this manuscript.

References

[1] State of New York Department of Mental Hygiene; *A Report to Gov. Hugh L. Carey on the Insanity Defense in New York.* New York, 1978. Pp. 8 and 9.

[2] *Myths and Realities: A Report of the National Commission on the Insanity Defense:* A Project of the National Mental Health Association. Arlington, Va. 1983. Pp. 5 and 6.

Reprint requests to: Ronald Mark Stewart, MD, 277 Waterman Street, Providence, RI 02906

Seeking referrals for

Multiple Clinical Studies

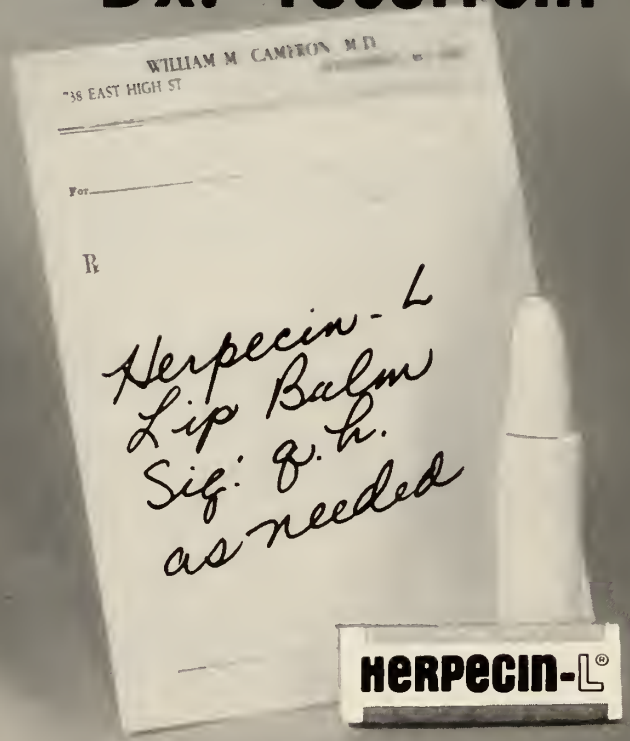
Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

LAW OFFICE
OF
HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

PHYSICIAN WANTED
TO COVER NIGHTS, WEEKENDS, AND HOLIDAYS
INSTITUTE OF MENTAL HEALTH

A 300-bed psychiatric hospital in Cranston is seeking physicians who are willing to work during off-hours to perform admissions of psychiatric patients and respond to medical and psychiatric emergencies. The duties are similar to those for a house medical officer.

The physician will work in collaboration with a qualified psychiatrist on administrative call.

70 hours/month
Salary: $300.00/night
Excellent sleeping quarters

Call the Medical Director at
464-2458

NOW UNDER DEVELOPMENT
at
ASHLEY DOWNS
BIOPHARMACEUTICAL LABS

An entire new line of **NONANIMAL SOURCE** Insulins
Pūrinsulin Human® ..... nonanimal rDNA source
Pūrinsulin Pork® ..... nonanimal rDNA source
Pūrinsulin Beef® ..... nonanimal rDNA source
Pūrinsulin Beef/Pork® ..... nonanimal rDNA source

Human Tissue Plasminogen Activator (tPA)
Plasminase® ..... chemically synthesized gene product

Human Erythroprotein (EPO)
Erythrōten® ..... chemically synthesized gene product

In R&D: Factor VIII; Interleukin-2; Growth Hormone

Ashley Downs Biopharmaceutical Laboratories
A NEW BIOTECH FACILITY
IN RHODE ISLAND

correspondences to:
Ashley Downs Biopharmaceutical Laboratories
909 North Main Street
Providence, RI 02904

DOCTORS WANTED

Like the Marines, we are also looking for a few good men (or women). However, we seek Board Certified Physicians, who are particularly proficient in patient history and physical examinations.

Medical Assessment Programs, with medical facilities in Boston and Springfield, Mass., and in Providence, R.I., provides comprehensive independent medical examinations for Workers' Compensation, Liability and Bodily Injury patients.

Full and Part-time positions available. Hours are Monday through Friday 9 to 5. No nights and no weekends.

Excellent benefits and salary.

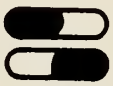
Call Dr. Smith at (617) 449-8201.

Medical Assessment Programs
32 Fremont St.
Needham Heights, MA 02194

Thalidomide and D.E.S.
(They could happen again.)

Sometimes even the most promising drug may have unexpectedly adverse reactions in patients. Pre-market testing identifies most toxic drugs before release for patient-care use, but not all. Toxicity in some drugs can only be determined through adverse reactions detected among a larger number of patients over a longer period of time.

The plain truth is that a patient's health may be at risk. Adverse drug reactions cause death in approximately 30,000 patients annually in the United States alone. So, if you suspect an adverse drug reaction, please report it promptly. We may all live longer because you did.



The Adverse Drug Reaction Reporting Project
of the Rhode Island Department of Health

To report an ADR by phone, call **456-ADRS** weekdays between 9 and 5. To receive mailing forms and additional information, call the Health Department at 277-2901.

Acute Renal Failure With Anuria Caused by Aortic Thrombosis and Bilateral Renal Artery Occlusion. A Report of Two Cases

Atherosclerosis and a Superimposed Hypercoagulable State Frustrated Successful Treatment in Both Cases

Richard I. Fogel, MD
Raymond G. Endreny, MD
John J. Cronan, MD
Joseph A. Chazan, MD, FACP

The purpose of this report is to describe two elderly patients who developed thrombosis of the aorta and bilateral renal occlusion which resulted in acute renal failure with anuria. Both patients had severe atherosclerosis which appeared to be the major factor responsible for the occlusion, but each had a predisposing "hypercoagulable" factor which may have been responsible for the thrombosis.

Richard I. Fogel, MD, was a Brown University Medical Science student while working on this paper. He is presently a resident at the University Hospital, Boston, Massachusetts.

Raymond G. Endreny, MD is an Assistant Clinical Professor at Brown University Program in Medicine.

John J. Cronan, MD is an Assistant Clinical Professor, Diagnostic Radiology at Brown University Program in Medicine and a radiologist with Rhode Island Hospital, Providence, RI.

Joseph A. Chazan, MD, FACP is Co-Director of Division of Renal Diseases, Rhode Island Hospital and an Associate Clinical Professor at Brown University Program in Medicine.

From the Department of Medicine, Division of Renal Diseases, and the Department of Radiology, Special Procedures Division, Rhode Island Hospital, and the Division of Biological and Medical Sciences, Brown University, Providence, Rhode Island.

Case Reports

Case 1. A 78-year-old female with a past history of diabetes mellitus and hypertension was admitted to the hospital because of left foot pain. An aortogram (Figure 1) performed from the left femoral approach revealed diffuse atherosclerosis of the abdominal aorta with a 3 cm aneurysm involving the distal abdominal aorta. A high-grade stenosis (less than 5 mm) of the right mid renal artery was present. Severe atherosclerotic stenosis involved the left superficial femoral artery proximally. The creatinine prior to the arteriogram was 0.9 mg per cent. Subsequently, a left femoral popliteal artery bypass was performed. Five days later the creatinine was 1.1 mg per cent. Six days later (11 days after surgery) the patient complained of pleuritic chest pain and hemoptysis. A ventilation perfusion lung scan indicated a high probability of pulmonary embolism. Heparin treatment was begun. Four days later the pulse in the left foot disappeared and a thrombectomy of the graft was performed. On the 16th postoperative day the patient excreted no urine. The creatinine was 3.7 mg per cent. The platelet count, which had been 220,000/ml on admission, fell to 40,000/ml and then 25,000/ml. A 99^{m} Tc-DTPA renal scan revealed absent bilateral renal perfusion. A repeat aortogram re-

Fig 1. Abdominal aortogram from the left femoral approach demonstrated diffuse atherosclerosis, a 3 cm aneurysm at the aortic bifurcation, and moderate right renal artery stenosis.

vealed multiple aortic intraluminal filling defects consistent with thrombi and complete occlusion of both renal arteries (Figure 2). The extensive nature of the thrombotic disease coupled with the patient's general clinical condition precluded surgical intervention. The patient expired on the 17th postoperative day. Autopsy revealed organizing thrombus involving the abdominal aorta at the level of the renal arteries with bilateral renal infarcts.

Case 2. A 68-year-old male with diffuse atherosclerosis and previous femoral popliteal bypass surgery was admitted to the hospital because of shortness of breath, agitation, and anuria. During the preceding 5 days the patient experienced intermittent claudication and one day of lower abdominal pain associated with weakness, nausea, and diaphoresis.

Physical examination revealed an acutely ill man with evidence of pulmonary edema and atrial fibrillation. Renal ultrasound scan revealed no evidence of hydronephrosis. The left kidney was somewhat smaller than the right kidney. A 99^{m} Tc-DTPA renal scan revealed no activity in the aorta below the upper abdomen. Kidney perfusion was not seen. Digital subtraction angiography performed via an inferior vena cava injection revealed thrombosis of the aorta above

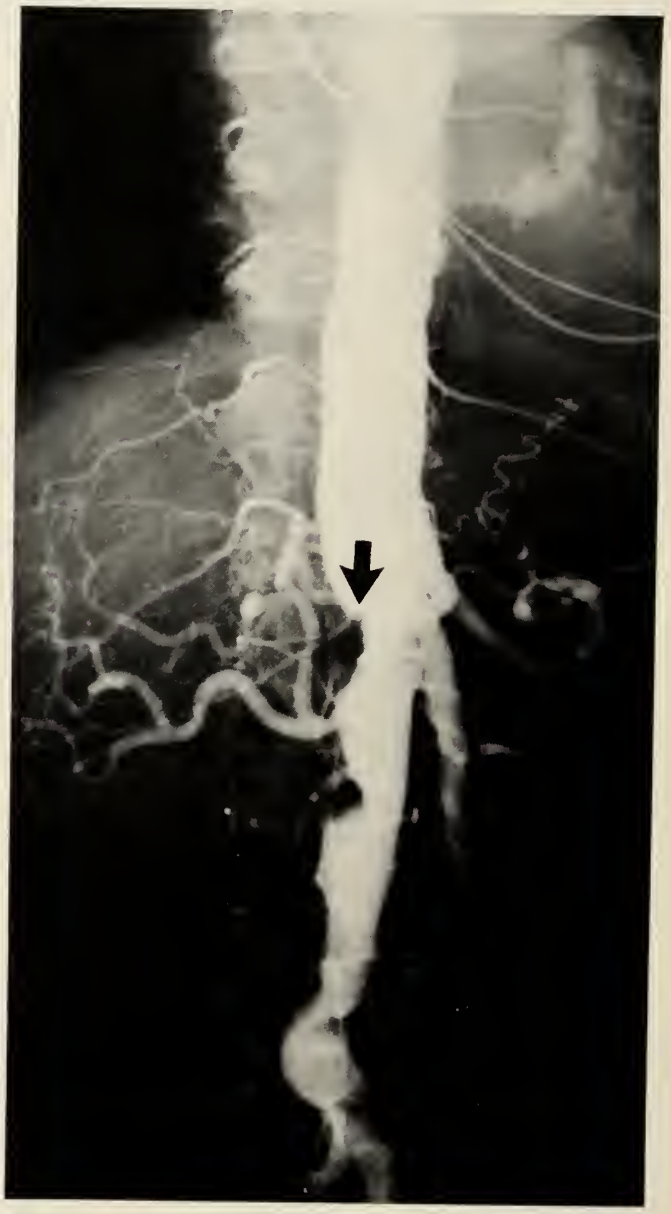


Fig 2. Repeat aortography demonstrates acute intraluminal filling defects consistent with thrombus. The renal arteries are not seen (arrow at level of renal arteries).

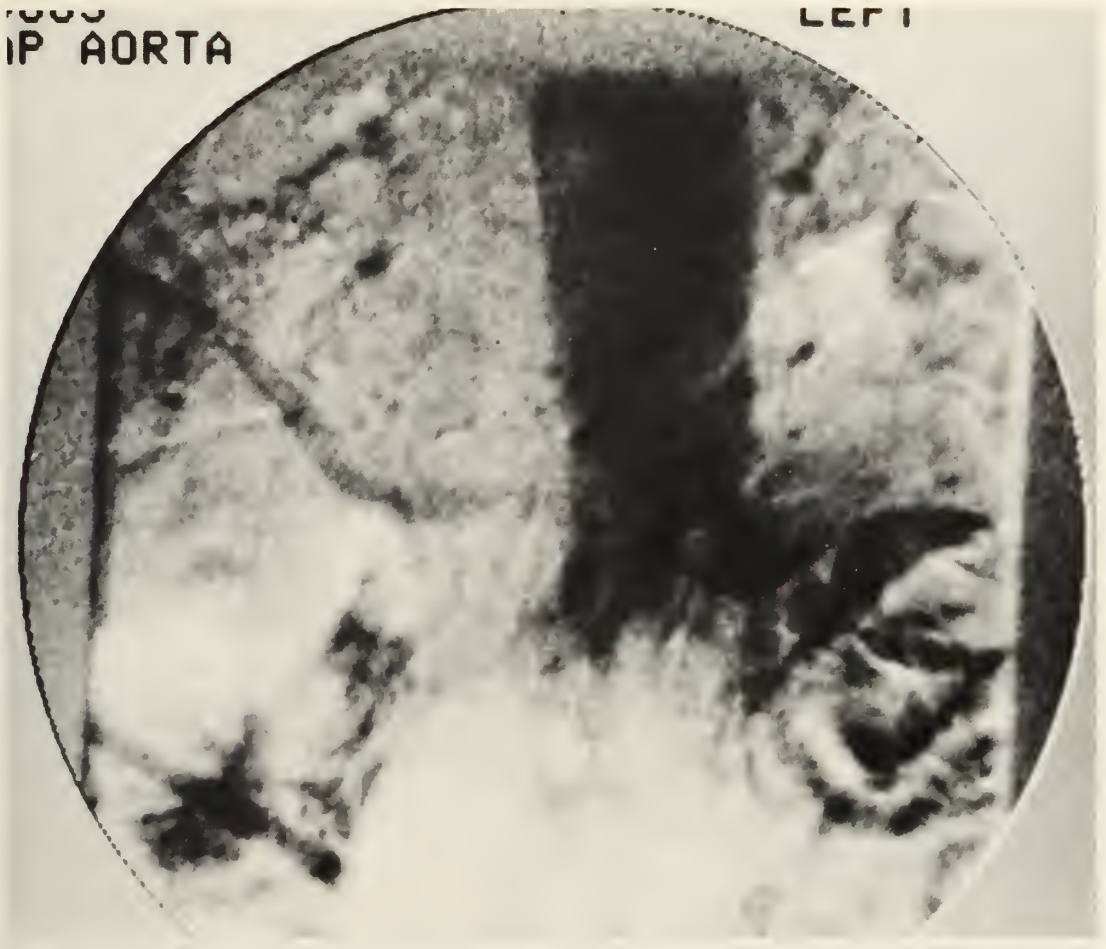


Fig 3. Digital subtraction aortogram following a venous injection demonstrated total occlusion of the suprarenal abdominal aorta. The kidneys were not seen on later films.

the renal arteries (Figure 3). The hematocrit was 60 per cent, and the platelets appeared to be normal. The patient secreted no urine, and the creatinine which was 1.8 mg per cent on admission rose to 11 mg per cent. Hemodialysis was instituted. However, when gastrointestinal hemorrhage and left upper extremity paralysis occurred and all supportive therapy was discontinued, the patient expired. No autopsy was performed.

Discussion

Causes for acute bilateral renal artery occlusion include trauma,[1,2] complications associated with surgery of the renal arteries,[3,5] renal emboli,[6-8] diffuse atherosclerosis[9-13] and hypercoagulable state.[14-17] Although renal artery stenosis or unilateral occlusion is a common clinical occurrence, acute renal failure from this cause is distinctly uncommon since the arterial occlusion is rarely both complete and bilateral.

Diagnostic evaluation of acute renal failure necessitates evaluation of a primary renal, pre-renal, or post-renal process. Renal ultrasound scanning has proven itself acceptable in most cases as a survey technique for post-renal (obstructive) etiologies. Radionuclide scanning traditionally has been utilized to assess the possibility of a pre-renal deficit accounting for renal failure. Recently some consideration has been given to Doppler ultrasound as a non-invasive technique to assess blood flow. Angiography, employing either cut film or digital data acquisition, can provide confirmatory invasive evaluation of renal artery blood flow.

In the clinical setting of severe atherosclerotic disease and sudden onset of acute renal failure, an ultrasound examination would allow one to exclude quickly and non-invasively the possibility of post-renal hydronephrosis. The absence of hydronephrosis would then warrant evaluation of the vascular system. Digital subtraction angiog-

raphy or radionuclide scanning would provide for immediate assessment of the pre-renal arterial status. Doppler ultrasound may prove to be of value in this setting.

The two patients described in this report had severe diffuse atherosclerosis and thus had potential for a low flow state. The superimposition of a "hypercoagulable" state could then result in thrombosis. The potential for this "hypercoagulable" state existed in both patients. Thrombocytopenia secondary to heparin therapy[16, 17] in Case 1 and erythrocythemia (hematocrit of 60) in Case 2. The age, general condition, and severity of the atherosclerosis precluded surgical intervention in these patients. However, in general, in the presence of this diagnosis, surgical intervention should be contemplated. Successful revascularization of the renal arteries has been described after 18 hours, 20 hours, and 38 days.[11-13] Limited experience has been reported with thrombolytic agents, which may offer a nonoperative treatment.[18]

Summary

Two patients who presented with acute renal failure and anuria secondary to aortic thrombosis and bilateral renal artery occlusion are described. Both patients had severe diffuse atherosclerosis with low flow states and may have developed intravascular clotting because of a superimposed hypercoagulable state. In one patient the hypercoagulable state was associated with heparin therapy and in the second with erythrocythemia. The severity of the atherosclerosis in these patients precluded surgical intervention. However, prompt clinical consideration and imaging documentation of this disease process might allow initiation of surgical or thrombolytic therapy in patients with less severe disease.

References

1 Steiness IB, Thaysen JM: (1965) Bilateral traumatic renal artery thrombosis. Lancet 1:527-529.

2 Lohse JR, Bothan RJ, Waters RF: (1982) Traumatic bilateral renal artery thrombosis: case report and review of literature. Jrnl of Urology 127:522-525.

3 Johansen K, Voci V, Cohen D, Feet P: (1981) Acute bilateral renal artery occlusion. Arch Surg 116:1232-1235.

4 Baciewicz FA: (1982) Bilateral renal artery thrombotic occlusion — a unique complication following removal of a transthoracic intraaortic balloon. Ann Thoracic Surg 33:631-34.

5 Burdick JF, Helikson MA, Hudak ML, Williams GM: (1982) Revascularization for bilateral renal artery occlusion after umbilical artery catheterization. Surgery 91:650-655.

6 Duncan DA, Dexter RN: (1962) Anuria secondary to bilateral renal artery embolism. N Engl J Med 266:971-973.

7 McGonigle RJS, Trafford JAP, Sharpstone P, Tapson JS: (1979) Survival after bilateral renal artery occlusion. Brit Med J 2:1261-1262.

8 Lessman RK, Johnson SF, Coburn JW, Kaufman JJ: (1978) Renal artery embolism. Clinical features and long-term follow-up of 17 cases. Ann Intern Med 89:477-482.

9 Wasser WG, Krakoff LR, Haimov M, Gladman S, Mitty HA: (1981) Restoration of renal function after bilateral renal artery occlusion. Arch Int Med 141:1647-1651.

10 Besarab A, Brown RS: (1976) Reversible renal failure following bilateral renal artery occlusive disease. JAMA 235:2838-2841.

11 Hamilton PB, Philips RA, Miller A: (1948) Duration of renal ischemia required to produce uremia. Am J Physiol 152:517-522.

12 Love L, Bush IM: (1968) Early demonstration of renal collateral arterial supply. Am J Roentgenology 104:296-301.

13 Hertzer NR, Montie JE, Hall PM, Bunowsky LM: (1976) Revascularization of the kidney after occlusion of the aorta and both renal arteries. Surgery 79:52-56.

14 Nicolau IB, Zurita JMC, Guzman AB, et al: (1982) Essential thrombocytosis with acute renal failure due to bilateral thrombosis of the arteries and veins. Nephron 32:73-74.

15 Thomas JM, Pfaff W: (1967) Acute anuria secondary to renal artery stenosis. Ann of Surgery 183:293-295.

16 Cimo PL, Moake JL, Weinger RS, Ben-Menachem Y, Khalil KG: (1979) Heparin induced thrombocytopenia with a platelet aggregating factor and arterio-thrombosis. Am J Hematol 6:125.

17 King DJ, Kelton JG: (1984) Heparin-associated thrombocytopenia. Ann Int Med 100:535-540.

18 Cronan JJ Jr, Dorfman GS: (1983) Low dose thrombolysis: a nonoperative approach to renal artery occlusion. J of Urology 130:757-759.

Address for communications and reprint requests to: Joseph A. Chazan, MD, FACP, Division of Renal Diseases, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02902.

PERIPATETICS

Dr Paul Koch, a Warwick ophthalmologist, and **Dr Joseph DiBenedetto,** Providence oncologist, have been named to the board of directors of Health Care Review, Inc., the medical review organization for the Medicare program in Maine and Rhode Island.

• • •

The faculty of the 1987 Update and Training in Anatomy, Pathological Anatomy, and Oncology, held at the University of Ancono in Italy, included as a guest lecturer **Dr Salvatore K. Allegra,** director of pathology at St. Joseph Hospital.

• • •

Dr Gerald Marsocci, a general and vascular surgeon, has been appointed director of the Division of General Surgery at Roger Williams General Hospital in Providence.

• • •

At the 27th annual American Heart Association Conference on Cardiovascular Disease Epidemiology in South Carolina, a paper, "Neonatal Salt Taste and Infant Blood Pressure," was presented by **Dr Stephen Zinner,** head of Infectious Diseases at Roger Williams General Hospital and professor of medicine at Brown University. The paper was the result of a two-year research project conducted in conjunction with Stephen McGarvey, PhD; Lewis Lipsitt, PhD; Bernard Rosner, PhD; and **Dr William Oh.**

• • •

Dr Hugo Taussig was honored with the Warren Williams Speaker's Award for his outstanding contributions to psychiatry at the 140th Annual Meeting of the American Psychiatric Association in Chicago, Illinois. **Dr Taussig** donated his award to Amnesty International.

Dr Allan M. Deutsch, radiologist-in-chief at The Miriam Hospital, has been elected to fellowship in the American College of Radiology. **Dr Deutsch** was elected to fellowship by the board of chancellors of the college in Virginia. The honor was given to him based on his outstanding contributions and services to radiology.

• • •

The "Teacher of the Year" award was presented to **Dr Steven M. Opal,** Infectious Disease Division at Memorial Hospital of Pawtucket, during its recent graduation ceremonies for residents and fellows. **Dr Opal** was selected by the house staff to receive this award because of his enthusiastic approach to his subspecialty and a desire to share his knowledge with others.

• • •

One of thirty orthopedic surgeons, **Dr Jean A. Marcellot** has been asked to travel with the US Men's Olympic Ski Team during their training in Europe. **Dr Marcellot** is on the staff at The Woonsocket Hospital.

• • •

Dr David B. Stoll, Chief of Hematology/Oncology at The Woonsocket Hospital, has been named Assistant Clinical Oncologist at Rhode Island Hospital. **Dr Stoll,** a past vice president of medical affairs for the American Cancer Society, Northeastern Division, has been elected president of that organization for 1987.

• • •

The American Academy of Facial Plastic and Reconstructive Surgery (AAFPRS) has named **Dr Hani Mahmoud Zaki,** St. Joseph Hospital Department of Otolaryngology, as a fellow.

• • •

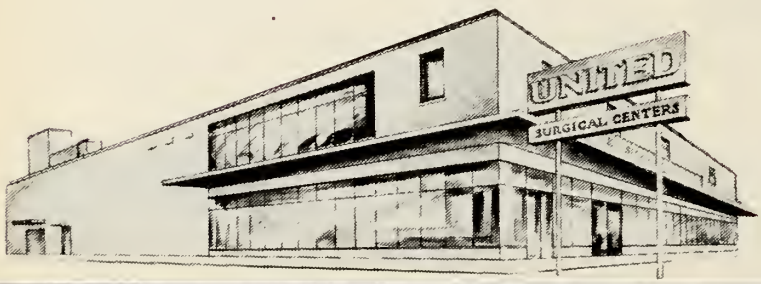
Recently Board Certified in the subspecialty of Nephrology by the American Board of Internal Medicine was **Dr Steven B. Zipin,** a nephrologist on The Woonsocket Hospital Courtesy Staff. **Dr Zipin** is also a Clinical Assistant Professor in Medicine at Brown University.

There must be a good reason why

UNITED SURGICAL CENTERS

The Professionals in Home Health Care Equipment

we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.



We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.

(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

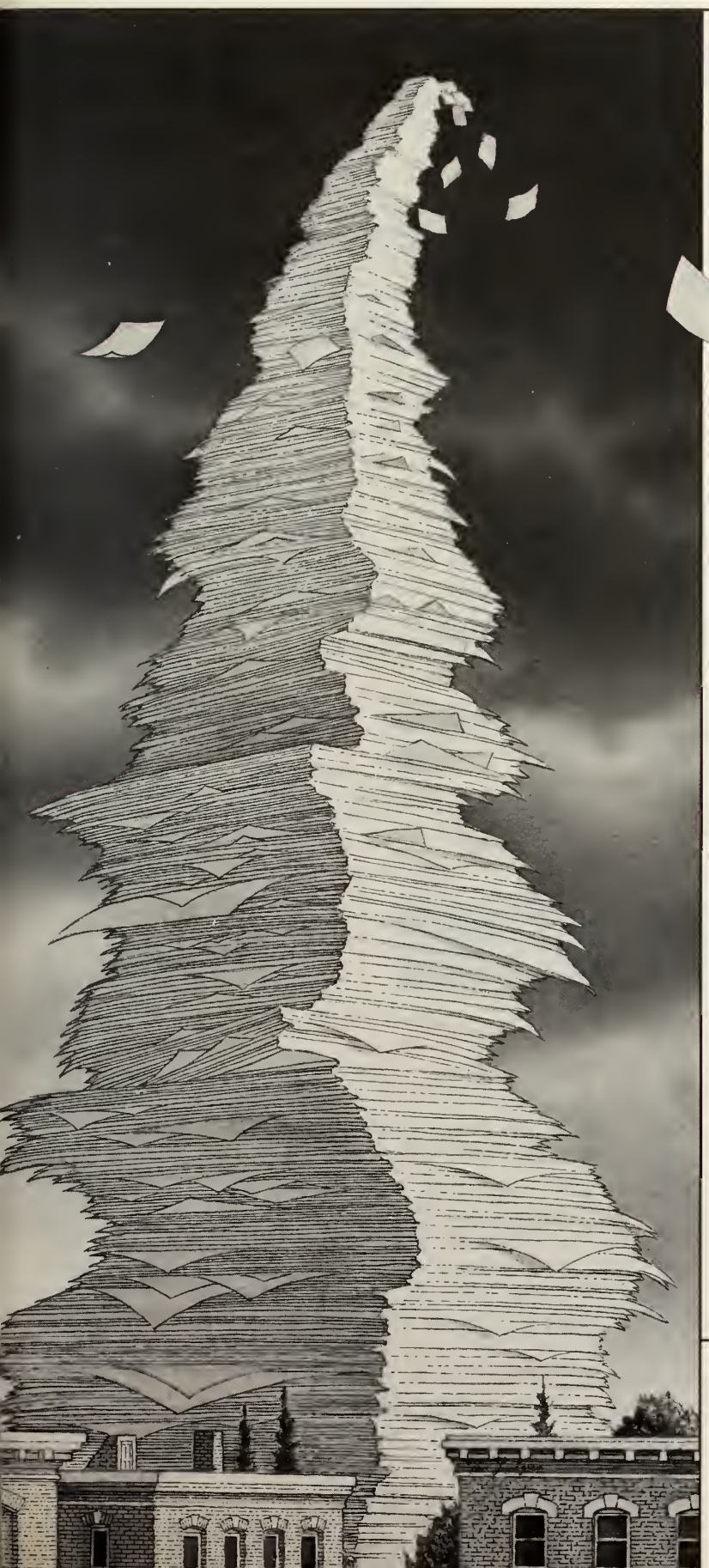
COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

1-800-521-7974

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

FINANCE YOUR INVESTMENTS WITHOUT INVESTING A LOT OF YOUR TIME.



When you've set your sights on a new medical office, computer system, or piece of real estate, your Private Banker at Bank of New England-Old Colony can make financing your investment as easy for you as writing a prescription.

No one understands your specialized needs and professional situation—and the way through the maze of tax laws, loan procedures, and red tape attendant with meeting your financing objectives—better than your Private Banker. Once your plan is in motion, this special banking relationship will continue to work to your benefit with ongoing timely and accurate financial counseling and direction. And our expert assistance is available to you without additional fees or extra charges of any kind.

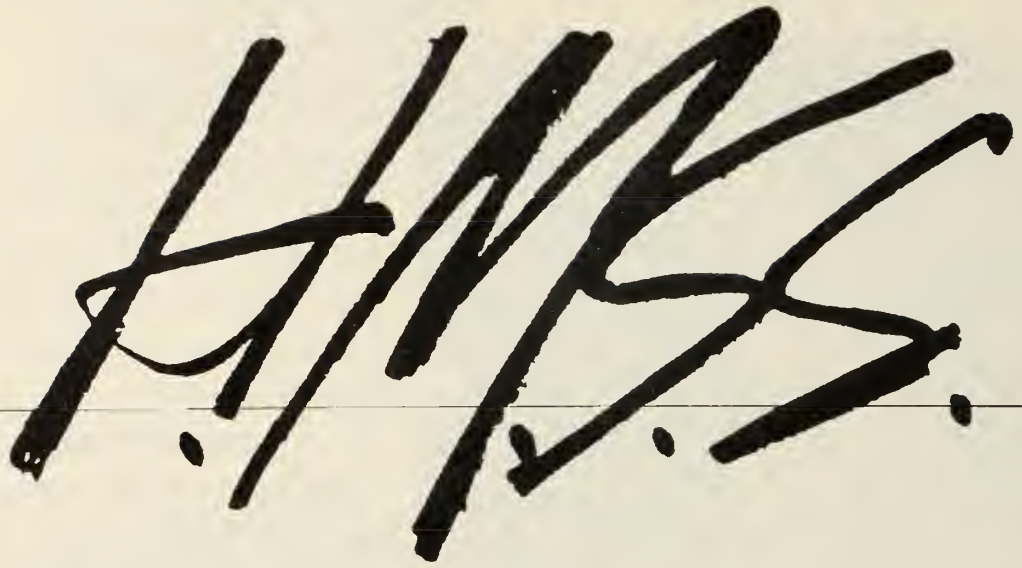
With a responsive expert handling every detail of your financial requirements, you can continue doing what you do best without missing a beat.

Call Dick Boenning, Director of Private Banking, at 575-2050.

PRIVATE BANKING

BANK OF NEW ENGLAND®
OLD COLONY

We take your financial goals personally.
Member FDIC



The AMA Hospital Medical Staff Section Tenth Assembly

DECEMBER 3-7, 1987
WESTIN PEACHTREE PLAZA
ATLANTA, GEORGIA

Represent your medical staff

For Information Contact:

Department of Hospital Medical
Staff Services
American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610
Phone (312) 645-4747 or 645-4753

HAVE YOU HEARD?

Practitioners should assume that all adults seeking medical examinations for participation in strenuous sports probably have coronary artery disease. Dr Henry S. Miller, Wake Forest University physician, states that the high incidence of coronary artery disease and hypertension in the United States demands this assumption. He warned physicians to be suspicious about all common medical problems associated with the patient's age, especially those related to sudden death. According to Miller, professor of medicine and director of cardiology at Wake Forest University Bowman Gray School of Medicine, physicians should never assume that an individual who has participated in a sport for which he or she is being examined is free of cardiovascular disease.

"Most sudden deaths in athletes have occurred in individuals who have played the specific sport for 5-10 years or have been running 4-5 years," he explained. "It is also important to realize that cardiovascular abnormalities associated with congenital disease may worsen with age and that the intensity with which a person exercises usually increases with age." Miller maintains that simple practical methods can identify most cardiovascular problems such as a good current medical history.

• • •

Burroughs Wellcome Co will pursue further development of its antidepressant drug Wellbutrin® (bupropion hydrochloride) through a new clinical program which will begin shortly. Evaluations will continue on the incidence of seizures associated with the use of the drug in the general population of depressed patients. Wellbutrin® was approved by the Food and Drug Administration in 1985 for the treatment of patients who did not respond to or could not tolerate other antidepressants. In February 1986, prior to full-scale marketing, Burroughs Wellcome voluntarily withdrew Wellbutrin® because several non-depressed patients in a clinical trial evaluating it for the treatment of the eating disorder bulimia experienced seizures. Since that time the company has been involved in negotiations with regulatory and other agencies regarding the development of the drug. Three thousand patients nationwide are expected to be involved in the new clinical trial with results not available until late 1988. Patients currently receiving the drug through other programs will continue to receive it while the new study in underway.

• • •

A report in July's *Archives of General Psychiatry* suggests that a test may soon be available allowing clinicians to predict the course of schizophrenia or to identify patients who could remain stable on lower drug doses. Jeffrey A. Lieberman, MD, of Long Island Jewish Medical Center, Glen Oaks, NY, and colleagues studied 34 stable schizophrenics on drug therapy who were given a "challenge" test with methylphenidate, a drug that selectively inhibits neuronal uptake of the neurotransmitter dopamine, high levels of which have been implicated in schizophrenia. Specific measures of behavioral, cardiovascular, and neurologic response to the test were associated with time and tendency to relapse after withdrawal of drug therapy, the study says. "These measures may be potentially useful in the identification of candidates for (drug) withdrawal and/or dosage reduction strategies," it concludes.

• • •

According to Dr Ernest W. Johnson, sports medicine authority, a common misconception about sports injury inflammations such as tennis elbow and shin splints is that rest should be prescribed. Rather, he recommends heavy resistance exercises that actually speed up relief even during the painful acute phase. Johnson, professor and chair of the department of physical education at Ohio State University in Columbus, reports that many common sports-related inflammatory reactions are identified by localized pain and vigorous muscle contractions. Once X-ray studies or

bone scans have ruled out a fracture as a potential cause of pain, the inflammation is best treated with progressive resistance exercises and anti-inflammatory medications.

Johnson does not recommend rest because pain will recur when activity is resumed. It is one of the most overutilized treatments for athletic injury pain and should be reserved for injuries such as second- and third-degree ankle sprains and some stress fractures. Johnson recommends using a combination of medications to reduce pain during the two- to six-weeks necessary for the inflammation to become pain free. A combination of aspirin and codeine is particularly effective for short-term pain relief.

• • •

At the American Diabetes Association Annual Meeting, held in Indiana from June 6 to 9, Novo Research Institute scientists announced the discovery of a series of new insulin molecules with unique and improved properties compared to existing insulin preparations. The first products, extra-rapid-acting insulins and soluble long-acting insulins, have been designed to overcome the present limitations of subcutaneous insulin absorption. According to Ulrik V. Lassen, Chief Science Officer at Novo, pancreatic insulin was never intended for subcutaneous injection. After injection, the extra-rapid-acting insulins are absorbed much more quickly from subcutaneous tissue. Injection prior to a meal will mimic the normal rapid and short-lived insulin secretion found in non-diabetics. The new long-acting insulins mimic the normal basal insulin secretion in a more predictable manner with less variation than present crystalline insulin suspensions. Research is still in the beginning stages with product availability not projected for at least five years. Results from the first human trial conducted by Dr. David Owens in Cardiff, Wales confirm the unique biological and physico-chemical properties of these insulins.

• • •

Calan® and Calan SR®, cardiovascular drugs which treat high blood pressure, angina and certain heart rhythm disorders, is being made available to indigent hypertensive patients by G. D. Searle Co of Skokie, Illinois. This is part of the company's "Calan® Program For Patients In Need." Studies indicate that about 100,000 individuals suffer from hypertension but drug therapy is unaffordable for them. Without treatment, one-third of these people could suffer a fatal stroke within the year. Since the beginning of Searle's pilot program last February, over 13,000 physicians nationwide are participating.

• • •

Eastman Kodak Company has announced that it will file an application with the FDA for approval to begin clinical studies on a new test that can simultaneously detect the antibodies to HIV (the causitive agent of AIDS) and HTLV-1 (the agent associated with adult T-cell leukemia/lymphoma). John R. Zeman, vice president and general manager of Kodak's Clinical Products Division projects that the new test, developed by Cellular Products, Inc, of Buffalo, NY, will largely reduce cost to blood banks. Two separate tests are currently performed to detect these antibodies.

• • •

A two-year pilot study on a new treatment for a common form of leukemia is underway at St. Andrews University in Scotland. A treatment utilizing lower doses of existing drugs to provide a multiplier effect to induce leukemia cells to revert to normal, healthy cells has been developed by the research team headed by Professor Brynmor Thomas and Dr Andrew Riches. High drug doses aimed at killing off diseased cells is part of the present treatment, which carries the danger of harming healthy cells. The intent of the study and clinical trials is to find a treatment for myeloid leukemia, a common form of the disease affecting mostly adults.

• • •

August's *Archives of Internal Medicine* states that even with studies showing 25 to 50 per cent of patients admitted for acute hospital care are malnourished, affecting their recovery, doctors are not being taught to recognize this problem. Patients admitted to an acute medical service before and after their doctors were taught to recognize nutritional deficiency early and provide appropriate intervention were studied by Ronenn Roubenoff, MD, of the Johns Hopkins Hospital, Baltimore, and colleagues. In the initial study phase, the house staff correctly identified only two of 16 malnourished patients. After training, however, 14 patients at nutritional risk all were identified correctly using a simple screening device requiring only routine admission data. Physician education as a cost-effective and sensible approach to the problem was suggested by the authors.

BOOKS RECEIVED

Healing Into Life and Death by Stephen Levine, Doubleday and Company, Inc., New York, 1987, 264 pp., $8.95.

" . . . a vital contribution to the literature of coping with disease, be it terminal, chronic, emotional, or spiritual. An invaluable synthesis of traditional Western medicine and Eastern meditative philosophy . . . proposes to draw together the often warring parties of the mind and body to allow life, death, sickness, and health to be experienced on a higher, more productive level."

The Health Century, A companion to the PBS television series, by Edward Shorter, PhD, Doubleday and Company, Inc., New York, 1987, 320 pp., $21.95.

"documents medical breakthroughs — many of which were enabled by the unique partnership of government, academia, and industry. . . . Focusing on key researchers and scientists . . . truly a ground breaking volume."

Neurology: Problems In Primary Care by James L. Bernat, MD and Frederick M. Vincent, MD, Medical Economics Company, Inc., Oradell, NJ, 1987, 656 pp., $39.95.

"Problem oriented . . . begins with the difficult topics of diagnostic tests and physical diagnosis, which are presented with ease and with interest to the reader. The most thorough guide now available in the diagnosis and management of commonly encountered neurologic disorders. Essential for the primary care physicians who need to keep abreast of all new developments in the treatment of common neurologic problems."

The Physician's Guide to Practice Location by State 1987-1988: Volume 1 (Alabama-Kentucky) by O. Sam Ashouri, MD, Doctors Publishing Inc., Jacksonville, Florida, 360 pp., $36.90.

"produced to provide a comprehensive guide to all elements involved in physician practice locations throughout this country. It combines easy referencing with readability and personable approach."

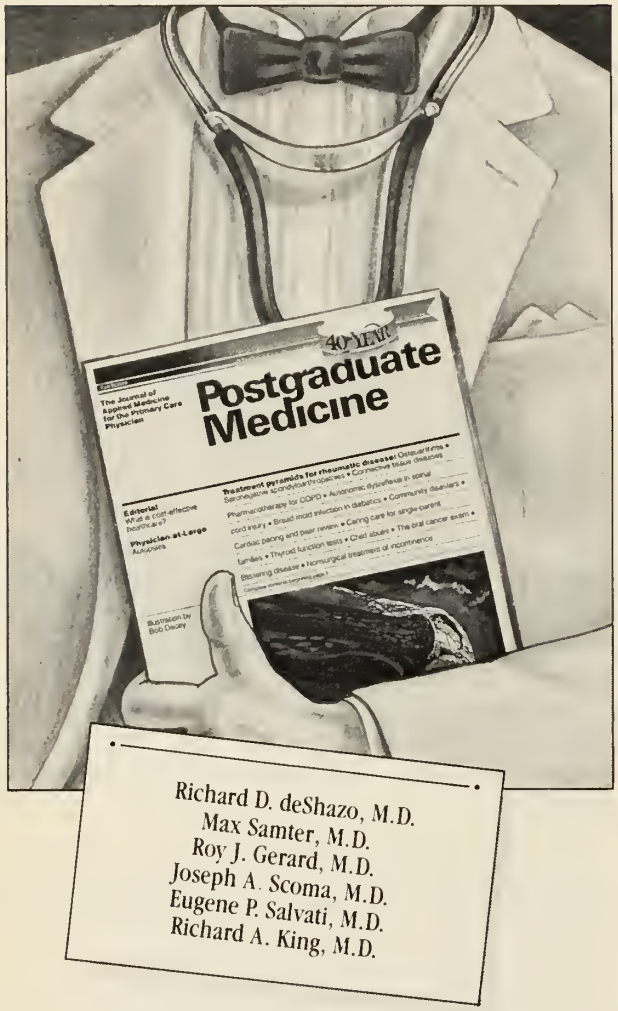
Physicians Observed: A Startling Examination of the Men and Women We Trust With Our Lives by David R. Slavitt, Doubleday and Company, Inc., New York, 1987, 268 pp., $17.95.

"demystifies the medical profession and offers a humanistic, insider's look at physicians — their goals and motivations, their pressures and frustrations . . . uses interviews and anecdotes . . . points out difficult decisions that doctors face every day . . . also discusses effects of malpractice suits on doctors and the loss of physicians' autonomy as government and insurance companies encroach on their turf . . . explores the educational process of a doctor and the positive effect that the increasing role of women in medicine has had."

Sickle-Cell Anemia and Thalassemia: A Primer For Health Care Professionals, Canadian Sickle Cell Society, St. John's, Newfoundland, Canada, 1987, 223 pp., $10.00.

"The object of the book is to present in a compact, inexpensive format an updated text on these common and life-threatening diseases."

FAMOUS PHYSICIANS ARE SHOWING UP FOR OUR 40th YEAR CELEBRATION.



Read Every Issue From Cover to Cover:

October
Symposium: Allergy . . . . . Richard D. deShazo, M.D. Coordinator
Special Article: Allergy 1947-1987 . . . . . Max Samter, M.D.

November 1
Symposium: Focus on Family Practice . . . . . Roy J. Gerard, M.D. Coordinator

November 15
Symposium: Colon & Rectal Disease . . . . . Joseph A. Scoma, M.D. Coordinator
Special Article: Colon & Rectal Disease 1947-1987 . . . Eugene P. Salvati, M.D.

December
Symposium: Genetic Diseases
Special Article: Genetics 1947-1987 . . . . . Richard A. King, M.D.

40th YEAR
Postgraduate Medicine

Every Issue is a Celebration of Clinical Information

CARAFATE®
(sucralfate)

BRIEF SUMMARY

CONTRAINDICATIONS
There are no known contraindications to the use of sucralfate.

PRECAUTIONS
Duodenal ulcer is a chronic, recurrent disease. While short-term treatment with sucralfate can result in complete healing of the ulcer, a successful course of treatment with sucralfate should not be expected to alter the post-healing frequency or severity of duodenal ulceration.

Drug Interactions: Animal studies have shown that the simultaneous administration of CARAFATE with tetracycline, phenytoin, or cimetidine will result in a statistically significant reduction in the bioavailability of these agents. This interaction appears to be nonsystemic in origin, presumably resulting from these agents being bound by CARAFATE in the gastrointestinal tract. The bioavailability of these agents may be restored simply by separating the administration of these agents from that of CARAFATE by two hours. The clinical significance of these animal studies is yet to be defined.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No evidence of drug-related tumorigenicity was found in chronic oral toxicity studies of 24 months' duration conducted in mice and rats at doses up to 1 gm/kg (12 times the human dose). A reproduction study in rats at doses up to 38 times the human dose did not reveal any indication of fertility impairment. Mutagenicity studies have not been conducted.

Pregnancy: Pregnancy Category B. Teratogenicity studies have been performed in mice, rats, and rabbits at doses up to 50 times the human dose and have revealed no evidence of harm to the fetus due to sucralfate. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when sucralfate is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS
Adverse reactions to sucralfate in clinical trials were minor and only rarely led to discontinuation of the drug. In studies involving over 2,500 patients, adverse effects were reported in 121 (4.7%). Constipation was the most frequent complaint (2.2%). Other adverse effects, reported in no more than one of every 350 patients, were diarrhea, nausea, gastric discomfort, indigestion, dry mouth, rash, pruritus, back pain, dizziness, sleepiness, and vertigo.

DOSAGE AND ADMINISTRATION
The recommended adult oral dosage for duodenal ulcer is 1 gm four times a day on an empty stomach.

Antacids may be prescribed as needed for relief of pain but should not be taken within one-half hour before or after sucralfate.

While healing with sucralfate may occur during the first week or two, treatment should be continued for 4 to 8 weeks unless healing has been demonstrated by x-ray or endoscopic examination.

HOW SUPPLIED
CARAFATE (sucralfate) 1-gm pink tablets are supplied in bottles of 100 and in Unit Dose Identification Paks of 100. The tablets are embossed with MARION/1712. Issued 3/84

References:
1. Grossman MI: *Scand J Gastroenterol* 58 (suppl 15):7-16, 1980.
2. Marks IN, in Hellemans J, Vantrappen G (eds): *Gastrointestinal Tract Disorders in the Elderly.* Edinburgh, Churchill Livingstone, 70-81, 1984.
3. Krentz K, Jablonowski H, in Hellemans J, Vantrappen G (eds): *Gastrointestinal Tract Disorders in the Elderly.* Edinburgh, Churchill Livingstone, 62-69, 1984.

Another patient benefit product from
PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC.
KANSAS CITY, MO 64137

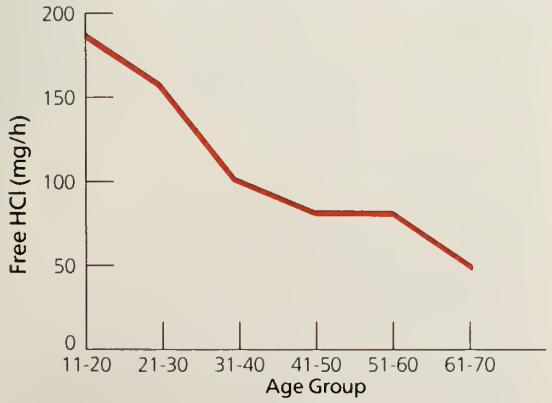
1595H7

Specialized ulcer therapy

When advancing age signals reduced acid secretion

If your duodenal ulcer patient is over 55, decreased mucosal resistance is more likely to cause an ulcer than hypersecretion of acid-pepsin.[1] A tendency toward lower acid secretion with advancing age has been shown.[2,3]

Declining gastric secretion and age[3]



CARAFATE® (sucralfate/Marion) makes sense as initial ulcer therapy for the elderly. Carafate provides ulcer healing rates comparable to H_2 antagonists without the risk of systemic side effects or drug interactions—an important benefit for older patients.

The unique, nonsystemic action of Carafate enhances the body's own ulcer healing ability, strengthening the mucosal structure as it protects damaged tissue from further injury.

When advancing age signals reduced acid secretion, choose the specialized ulcer therapy of safe, nonsystemic Carafate.

Nothing works like

CARAFATE®
sucralfate/Marion

Please see adjoining page for references and brief summary of prescribing information.

1595H7

There's never been a better time for her...

and PREMARIN®

Proven benefits beyond relief of vasomotor symptoms

No other estrogen proven effective for osteoporosis

Only conjugated estrogens tablets have established efficacy in both osteoporosis[1] and vasomotor symptoms* at 0.625 mg/day. No other estrogen, oral or transdermal, has established clinical evidence or minimum effective dose in both indications.

No estrogen proven safer

PREMARIN is the most extensively tested estrogen, with an unsurpassed record of long-term safety.
And clinical evidence shows a significantly reduced risk of endometrial hyperplasia when cycled with a progestin.[2]

PREMARIN®
(conjugated estrogens tablets)

Most trusted for more reasons

*PREMARIN is indicated for moderate-to-severe vasomotor symptoms

Please see following page for brief summary of prescribing information.

For moderate-to-severe vasomotor symptoms and for osteoporosis

PREMARIN®
(conjugated estrogens tablets)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

For atrophic vaginitis

PREMARIN®
(conjugated estrogens)

Vaginal Cream

0.625 mg/g

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION SEE PACKAGE CIRCULARS)*

PREMARIN® Brand of conjugated estrogens tablets, USP
PREMARIN® Brand of conjugated estrogens Vaginal Cream, in a nonliquefying base

1 ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA
Three independent, case-controlled studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case-controlled studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semi-annual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equi-estrogenic doses.
2 ESTROGENS SHOULD NOT BE USED DURING PREGNANCY
The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a nonsteroidal estrogen, have an increased risk of developing, in later life, a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1,000 exposures. Furthermore, a high percentage of such exposed women (from 30% to 90%) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb-reduction defects. One case-controlled study estimated a 4.7-fold increased risk of limb-reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb-reduction defects in exposed fetuses is somewhat less than 1 per 1,000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well-controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (conjugated estrogens, USP) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters. Tablets are available in 0.3 mg, 0.625 mg, 0.9 mg, 1.25 mg, and 2.5 mg strengths of conjugated estrogens. Cream is available as 0.625 mg conjugated estrogens per gram.

INDICATIONS AND USAGE: PREMARIN (conjugated estrogens tablets, USP). Moderate-to-severe *vasomotor* symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms and they should not be used to treat such conditions.) Osteoporosis (abnormally low bone mass). Atrophic vaginitis. Kraurosis vulvae. Female castration.

PREMARIN (conjugated estrogens) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae.

PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

Concomitant Progestin Use: The lowest effective dose appropriate for the specific indication should be utilized. Studies of the addition of a progestin for 7 or more days of a cycle of estrogen administration have reported a lowered incidence of endometrial hyperplasia. Morphological and biochemical studies of the endometrium suggest that 10 to 13 days of progestin are needed to provide maximal maturation of the endometrium and to eliminate any hyperplastic changes. Whether this will provide protection from endometrial carcinoma has not been clearly established. There are possible additional risks which may be associated with the inclusion of progestin in estrogen replacement regimens. (See PRECAUTIONS.) The choice of progestin and dosage may be important; product labeling should be reviewed to minimize possible adverse effects.

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (see Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Estrogens have been reported to increase the risk of endometrial carcinoma (see Boxed Warning). However, a recent large, case-controlled study indicated no increase in risk of breast cancer in postmenopausal women. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast, have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolaou smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention, such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Pre-existing uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not yet complete. If concomitant progestin therapy is used, potential risks may include adverse effects on carbohydrate and lipid metabolism.

The following changes may be expected with larger doses of estrogen:
a. Increased sulfobromophthalein retention.
b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.
c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T_4 by column, or T_4 by radioimmunoassay. Free T_3 resin uptake is decreased, reflecting the elevated TBG; free T_4 concentration is unaltered.
d. Impaired glucose tolerance.
e. Decreased pregnanediol excretion.
f. Reduced response to metyrapone test.
g. Reduced serum folate concentration.
h. Increased serum triglyceride and phospholipid concentration.

As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

Long-term, continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. However, in a recent, large case-controlled study of postmenopausal women there was no increase in risk of breast cancer with use of conjugated estrogens.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow, dysmenorrhea, premenstrual-like syndrome, amenorrhea during and after treatment, increase in size of uterine fibromyomata, vaginal candidiasis, change in cervical erosion and in degree of cervical secretion, cystitis-like syndrome, tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating, cholestatic jaundice, chloasma or melasma which may persist when drug is discontinued; erythema multiforme, erythema nodosum, hemorrhagic eruption, loss of scalp hair, hirsutism, steepening of corneal curvature, intolerance to contact lenses; headache, migraine, dizziness, mental depression, chorea, increase or decrease in weight, reduced carbohydrate tolerance, aggravation of porphyria, edema, changes in libido.

ACUTE OVERDOSAGE: May cause nausea and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of conjugated estrogens tablets, USP

1. *Given cyclically for short-term use only:* For treatment of moderate-to-severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 mg to 1.25 mg or more daily). The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible. Administration should be cyclic (eg, three weeks on and one week off). Attempts to discontinue or taper medication should be made at three- to six-month intervals.

2. *Given cyclically:* Osteoporosis. Female castration. Osteoporosis—0.625 mg daily. Administration should be cyclic (eg, three weeks on and one week off). Female castration—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control.

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of conjugated estrogens Vaginal Cream

Given cyclically for short-term use only: For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (eg, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three- to six-month intervals.

Usual dosage range: 2 g to 4 g daily, intravaginally, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

References:

1. Lindsay R, Hart DM, Clark DM: The minimum effective dose of estrogen for prevention of postmenopausal bone loss. *Obstet Gynecol* 1984;63:759-763. **2.** Studd JWW, Thom MH, Paterson MEL, et al: The prevention and treatment of endometrial pathology in postmenopausal women receiving exogenous estrogens, in Pasetto N, Paoletti R, Ambrus JL (eds): *The Menopause and Postmenopause*. Lancaster, England, MTP Press Ltd, 1980, chap 13.

© 1987 Ayerst Laboratories
All rights reserved

6437/587

Ayerst AYERST LABORATORIES
New York, NY 10017

In acute and chronic edema due to CHF

FOR PREDICTABLE CONTROL

- **Less potassium loss for a given amount of sodium excretion than with furosemide[1-3]**
- **Predictable dose response[4]**
- **Diuresis completed hours faster than with furosemide after oral dosing[5]**
- **Better GI absorption[6,7]**
- **Early evening dosing helps prevent nocturnal dyspnea**

As with all loop diuretics, excessive doses of BUMEX can lead to profound diuresis with water and electrolyte depletion, including hypokalemia, so serum electrolytes should be monitored.

Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets; 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

References: **1**. Flamenbaum W. *Am J Cardiol 57*(2):3BA-43A, 1986. **2**. Broter DC, Fox WR, Chennovasin P. *J Clin Pharmacol 21*: 599-603, 1981. **3**. Iber FL, Boum RA. *J Clin Pharmacol 21*: 697-700, 1981. **4**. Henning R, Lundvall O: *Eur J Clin Pharmacol 6*: 224-227, 1973. **5**. Physicians' Desk Reference, 40th ed. Oradell, NJ, Medical Economics Company, 1986, pp. 939, 1480. **6**. Pentikainen PJ, *et al*: *Br J Clin Pharmacol 4*:39-44, 1977. **7**. *Lasix, A Review*. Somerville, NJ, Hoechst-Roussel Pharmaceuticals, Inc., 1980

BUMEX®
(bumetanide/Roche)
0.5-mg, 1-mg and 2-mg scored tablets
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome
Almost equal diuretic response occurs after oral and parenteral administration of Bumex. If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity
CONTRAINDICATIONS: Anuria. Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion. Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment
WARNINGS: Dose should be adjusted to patient's needs. Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risk to the patients.
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma. Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance. Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients.
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity. Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved. The potential for ototoxicity increases with intravenous therapy, especially at high doses.
Patients allergic to sulfonamides may show hypersensitivity to Bumex.
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary. Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets.
Hyperuricemia may occur. Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency. Bumex may increase urinary calcium excretion.
Possibility of effect on glucose metabolism exists. Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes.
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions.
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions.
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously.
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics.
Probenecid should not be administered concurrently with Bumex.
Concurrent therapy with indomethacin not recommended.
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage.
Interaction studies in humans have shown no effect on digoxin blood levels.
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity.
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
Bumetanide may be excreted in breast milk.
Pediatric Use: Safety and effectiveness below age 18 not established.
ADVERSE REACTIONS: Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease).
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting.
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection.
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium. Although manifestations of the pharmacologic action of Bumex, these conditions may become more pronounced by intensive therapy.
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts. Increases in urinary glucose and urinary protein have also been seen.
DOSAGE AND ADMINISTRATION:
Oral Administration: The usual total daily dosage is 0.5 to 2.0 mg and in most patients is given as a single dose.
Parenteral Administration: Administer to patients (IV or IM) with GI absorption problem or who cannot take oral. The usual initial dose is 0.5 to 1 mg given over 1 to 2 minutes. If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day.
HOW SUPPLIED: *Tablets*, 0.5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescriptian Paks of 30, Tel-E-Dose™ cartons of 100. Imprint on tablets: 0.5 mg—ROCHE BUMEX 0.5; 1 mg—ROCHE BUMEX 1; 2 mg—ROCHE BUMEX 2.
Ampuls, 2 ml, 0.25 mg/ml, boxes of ten.
Vials: 2 ml, 4 ml and 10 ml, 0.25 mg/ml, boxes of ten.

P1 0985

Roche Laboratories
a division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

In acute and chronic edema due to CHF

A DIURETIC THAT GIVES YOU PREDICTABLE CONTROL

Bumex®
bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets; 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

Please see adjacent page for references and summary of product information.

Copyright © 1987 by Hoffmann-La Roche Inc. All rights reserved.

Rhode Island Medical Journal

December 1987
Volume 70, Number 12

The new Sayles Building at The Memorial Hospital
Pawtucket, Rhode Island

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

DEC 24 1987

CONTRIBUTIONS

533 The Pawtucket Heart Health Program:
I. An Experiment in Population-Based Disease Prevention

541 The Pawtucket Heart Health Program:
II. Evaluation Strategies

549 The Surgical History of Narragansett Bay

527 INDEX — VOLUME 70

529 EDITORIAL

531 EDITOR'S MAILBOX

There's more to Portable X-Ray Service than X-Rays.

Yes, our main business is to provide you with fast, efficient, diagnostic X-Ray services, but we have much more to offer . . . including a staff of people who really care.

- Diagnostic X-Ray Services
- EKG
- Holter-Monitoring*
- Ultrasound Services*
- Same day reporting
- 24 hour service
- Seven days a week

*by appointment only

We service the entire Greater Rhode Island area:

- Nursing and Convalescent Homes
- Shut-ins and Private Home Patients
- Post Surgical Patients

PORTABLE X-RAY SERVICE

OF RHODE ISLAND

Certified by the R.I. Department of Health. Reimbursement provided by Medicare, R.I. Blue Shield and Medical Assistance.

100 Highland Avenue Providence, R.I. 331-3996	120 Dudley Street Providence, R.I. 331-3996	154 Waterman Street Providence, R.I. 273-0450	38 Hamlet Avenue Woonsocket, R.I. 766-4224

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

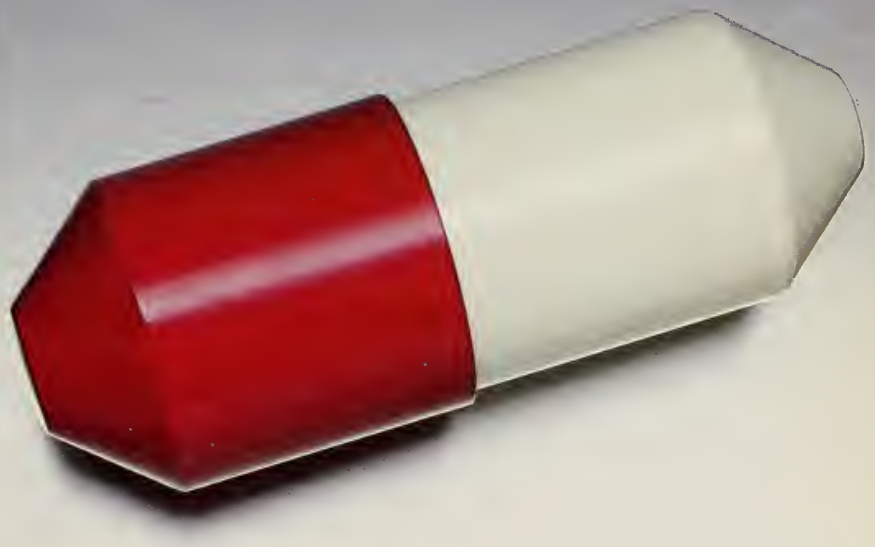
Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ L42

In Hypertension*... When You Need to Conserve K^+

Remember the Unique Red and White Capsule: Your Assurance of SK&F Quality

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).



Potassium-Sparing

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Over 20 Years of Confidence

The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

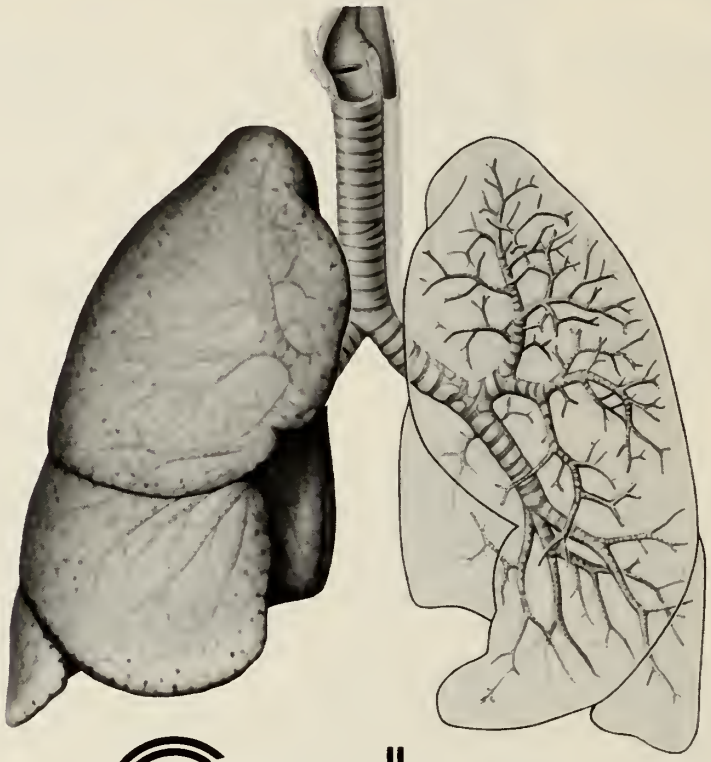
a product of

SK&F CO.

Carolina, P.R. 00630

© SK&F Co., 1983

Consider the causative organisms...



Ceclor®
cefaclor

250-mg Pulvules® t.i.d. offers effectiveness against the major causes of bacterial bronchitis

Haemophilus influenzae and *Streptococcus pneumoniae*
(ampicillin-susceptible and ampicillin-resistant)

Note: Ceclor is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Ceclor® (cefaclor)

Summary. Consult the package literature for prescribing information.

Indication: Lower respiratory infections, including pneumonia, caused by *Streptococcus pneumoniae, Haemophilus influenzae*, and *Streptococcus pyogenes* (group A β-hemolytic streptococci).

Contraindication:
Known allergy to cephalosporins.

Warnings:
CECLOR SHOULO BE AOMINISTEREO CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS PENICILLINS ANO CEPHALOSPORINS SHOW PARTIAL CROSS-ALLERGENICITY POSSIBLE REACTIONS INCLUOE ANAPHYLAXIS.

Administer cautiously to allergic patients.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It must be considered in differential diagnosis of antibiotic-associated diarrhea. Colon flora is altered by broad-spectrum antibiotic treatment, possibly resulting in antibiotic-associated colitis.

Precautions:
- Discontinue Ceclor in the event of allergic reactions to it.
- Prolonged use may result in overgrowth of nonsusceptible organisms.
- Positive direct Coombs' tests have been reported during treatment with cephalosporins.
- Ceclor should be administered with caution in the presence of markedly impaired renal function. Although dosage adjustments in moderate to severe renal impairment are usually not required, careful clinical observation and laboratory studies should be made.
- Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
- Safety and effectiveness have not been determined in pregnancy, lactation, and infants less than one month old. Ceclor penetrates mother's milk. Exercise caution in prescribing for these patients.

Adverse Reactions: (percentage of patients)

Therapy-related adverse reactions are uncommon. Those reported include:
- Gastrointestinal (mostly diarrhea): 2.5%.
- Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.
- Hypersensitivity reactions (including morbilliform eruptions, pruritus, urticaria, and serum-sickness-like reactions that have included erythema multiforme [rarely, Stevens-Johnson syndrome] or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever): 1.5%; usually subside within a few days after cessation of therapy. Serum-sickness-like reactions have been reported more frequently in children than in adults and have usually occurred during or following a second course of therapy with Ceclor. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.
- Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.
- As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.
- Rarely, reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, and somnolence have been reported.
- Other: eosinophilia, 2%; genital pruritus or vaginitis, less than 1%; and, rarely, thrombocytopenia.

Abnormalities in laboratory results of uncertain etiology
- Slight elevations in hepatic enzymes.
- Transient fluctuations in leukocyte count (especially in infants and children).
- Abnormal urinalysis; elevations in BUN or serum creatinine.
- Positive direct Coombs' test.
- False-positive tests for urinary glucose with Benedict's or Fehling's solution and Clinitest® tablets but not with Tes-Tape® (glucose enzymatic test strip, Lilly). [061787L]

PA 0709 AMP

©1987, ELI LILLY AND COMPANY CR-5005-B-849318

Lilly

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285.

Eli Lilly Industries, Inc
Carolina, Puerto Rico 00630

ZOVIRAX®
(acyclovir)
CAPSULES

Prevent genital herpes recurrences month after month with daily therapy.

(In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.)

Please see last page of this advertisement for brief summary of prescribing information

ZOVIRAX® (acyclovir) CAPSULES

Help free your patients from recurrences.

Daily therapy

Coping with genital herpes is rarely easy. For some, the worst part is the pain and discomfort of frequent attacks—month after month, year after year. For others, the emotional burden presents a more difficult problem, leading to social isolation, anxiety, and diminished self-esteem.

Prevent or reduce recurrences

Although your patients have to live with herpes, they shouldn't have to suffer. Daily therapy with ZOVIRAX CAPSULES can help free them from the cycle of recurrent genital herpes. For many, one capsule three times a day can suppress recurrences completely while on therapy.

Generally well tolerated

Daily therapy with ZOVIRAX CAPSULES is generally well tolerated. The most frequent adverse reactions reported during clinical trials were headache, diarrhea, nausea/vomiting, vertigo, and arthralgia.

The physical and emotional difficulties posed by genital herpes are unique for each patient. The frequency and severity of recurrent episodes, as well as the emotional impact of the disease, should be considered when selecting daily therapy with ZOVIRAX CAPSULES.

Please see brief summary of prescribing information on next page.

Prevent recurrences month after month*

ZOVIRAX® (acyclovir) CAPSULES

Brief Summary

INDICATIONS AND USAGE: Zovirax Capsules are indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.

The severity of disease is variable depending upon the immune status of the patient, the frequency and duration of episodes, and the degree of cutaneous or systemic involvement. These factors should determine patient management, which may include symptomatic support and counseling only, or the institution of specific therapy. The physical, emotional and psycho-social difficulties posed by herpes infections as well as the degree of debilitation, particularly in immunocompromised patients, are unique for each patient, and the physician should determine therapeutic alternatives based on his or her understanding of the individual patient's needs. Thus Zovirax Capsules are not appropriate in treating all genital herpes infections. The following guidelines may be useful in weighing the benefit/risk considerations in specific disease categories:

First Episodes (primary and nonprimary infections — commonly known as initial genital herpes):

Double-blind, placebo-controlled studies have demonstrated that orally administered Zovirax significantly reduced the duration of acute infection (detection of virus in lesions by tissue culture) and lesion healing. The duration of pain and new lesion formation was decreased in some patient groups. The promptness of initiation of therapy and/or the patient's prior exposure to Herpes simplex virus may influence the degree of benefit from therapy. Patients with mild disease may derive less benefit than those with more severe episodes. In patients with extremely severe episodes, in which prostration, central nervous system involvement, urinary retention or inability to take oral medication require hospitalization and more aggressive management, therapy may be best initiated with intravenous Zovirax.

Recurrent Episodes:

Double-blind, placebo-controlled studies in patients with frequent recurrences (6 or more episodes per year) have shown that Zovirax Capsules given for 4 to 6 months prevented or reduced the frequency and/or severity of recurrences in greater than 95% of patients. Clinical recurrences were prevented in 40 to 75% of patients. Some patients experienced increased severity of the first episode following cessation of therapy; the severity of subsequent episodes and the effect on the natural history of the disease are still under study.

The safety and efficacy of orally administered acyclovir in the suppression of frequent episodes of genital herpes have been established only for up to 6 months. Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, Zovirax Capsules should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the human relevance of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given very high doses of acyclovir for short periods (see Carcinogenesis, Mutagenesis, Impairment of Fertility) should be borne in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus, this regimen should be considered only for appropriate patients and only for six months until the results of ongoing studies allow a more precise evaluation of the benefit/risk assessment of prolonged therapy.

Limited studies have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

CONTRAINDICATIONS: Zovirax Capsules are contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulation.

WARNINGS: Zovirax Capsules are intended for oral ingestion only.

PRECAUTIONS: General: Zovirax has caused decreased spermatogenesis at high doses in some animals and mutagenesis in some acute studies at high concentrations of drug (see PRECAUTIONS — Carcinogenesis, Mutagenesis, Impairment of Fertility). The recommended dosage and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION).

Exposure of Herpes simplex isolates to acyclovir *in vitro* can lead to the emergence of less sensitive viruses. The possibility of the appearance of less sensitive viruses in man must be borne in mind when treating patients. The relationship between the *in vitro* sensitivity of Herpes simplex virus to acyclovir and clinical response to therapy has yet to be established.

Because of the possibility that less sensitive virus may be selected in patients who are receiving acyclovir, all patients should be advised to take particular care to avoid potential transmission of virus if active lesions are present while they are on therapy. In severely immunocompromised patients, the physician should be aware that prolonged or repeated courses of acyclovir may result in selection of resistant viruses which may not fully respond to continued acyclovir therapy.

Drug Interactions: Co-administration of probenecid with intravenous acyclovir has been shown to increase the mean half-life and the area under the concentration-time curve. Urinary excretion and renal clearance were correspondingly reduced.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg given by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. In 2 *in vitro* cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive life-time bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weanling mice. Acyclovir was negative in another transformation system considered less sensitive.

In acute studies, there was an increase, not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of 100 mg/kg acyclovir in rats but not Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found after 5 days dosing in a dominant lethal study in mice. In 6 of 11 microbial and mammalian cell assays, no evidence of mutagenicity was observed. At 3 loci in a Chinese hamster ovary cell line, the results were inconclusive. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells *in vitro*), positive responses for mutagenicity and chromosomal damage occurred, but only at concentrations at least 400 times the acyclovir plasma levels achieved in man.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). At 50 mg/kg/day s.c. in the rat, there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day. No effect upon implantation efficiency was observed when the same dose was administered intravenously. In a rat peri- and postnatal study at 50 mg/kg/day s.c., there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites and live fetuses in the F_1 generation. Although not statistically significant, there was also a dose related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day, s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size. However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits, there were no drug-related reproductive effects.

Intraperitoneal doses of 320 or 80 mg/kg/day acyclovir given to rats for 1 and 6 months, respectively, caused testicular atrophy. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. Testicles were normal in dogs given 50 mg/kg/day, i.v. for one month.

Pregnancy: ***Teratogenic Effects:*** Pregnancy Category C. Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.), rat (50 mg/kg/day, s.c.) or rabbit (50 mg/kg/day, s.c. and i.v.). There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in animal studies, the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman. In nursing mothers, consideration should be given to not using acyclovir treatment or discontinuing breastfeeding.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS — Short-Term Administration: The most frequent adverse reactions reported during clinical trials were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Less frequent adverse reactions, each of which occurred in 1 of 298 patient treatments (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste and sore throat.

Long-Term Administration: The most frequent adverse reactions reported in studies of daily therapy for 3 to 6 months were headache in 33 of 251 patients (13.1%), diarrhea in 22 of 251 (8.8%), nausea and/or vomiting in 20 of 251 (8.0%), vertigo in 9 of 251 (3.6%), and arthralgia in 9 of 251 (3.6%). Less frequent adverse reactions, each of which occurred in less than 3% of the 251 patients (see number of patients in parentheses), included skin rash (7), insomnia (4), fatigue (7), fever (4), palpitations (1), sore throat (2), superficial thrombophlebitis (1), muscle cramps (2), pars planitis (1), menstrual abnormality (4), acne (3), lymphadenopathy (2), irritability (1), accelerated hair loss (1), and depression (1).

DOSAGE AND ADMINISTRATION: Treatment of initial genital herpes: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 10 days (total 50 capsules).

Chronic suppressive therapy for recurrent disease: One 200 mg capsule 3 times daily for up to 6 months. Some patients may require more drug, up to one 200 mg capsule 5 times daily for up to 6 months.

Intermittent Therapy: One 200 mg capsule every 4 hours, while awake, for a total of 5 capsules daily for 5 days (total 25 capsules). Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Patients With Acute or Chronic Renal Impairment: One 200 mg capsule every 12 hours is recommended for patients with creatinine clearance ≤ 10 ml/min/1.73/m^2.

HOW SUPPLIED: Zovirax Capsules (blue, opaque) containing 200 mg acyclovir and printed with "Wellcome ZOVIRAX 200" - Bottles of 100 (NDC-0081-0991-55) and unit dose pack of 100 (NDC-0081-0991-56).

Store at 15°-30°C (59°-86°F) and protect from light.

*In controlled studies, recurrences were totally prevented for 4 to 6 months in up to 75% of patients.

Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709

Copr © 1986 Burroughs Wellcome Co All rights reserved 86-ZOV-5

When you want to maximize the return on your significant income and assets, call a Hospital Trust Private Banker. For maximum strategies for your financial future.

Call Richard Kuntemeier, Senior V.P., 401-278-7648.

THE PRIVATE BANK

Hospital Trust

a BANK OF BOSTON company

Member FDIC

Equal Opportunity Lender

Rhode Island Medical Journal

December 1987
Volume 70, Number 12

EDITORIAL STAFF

Seebert J. Goldowsky, MD
Editor-in-Chief

Kimberly J. Allyn
Managing Editor

John E. Farrell, ScD
Managing Editor Emeritus

EDITORIAL BOARD

*Edward R. Feller, MD
Chairman

*Stanley M. Aronson, MD
Contributing Editor

*Maurice M. Albala, MD

Paul Calabresi, MD

Pierre M. Galletti, MD, PhD

Donald S. Gann, MD

*John F. W. Gilman, MD

*Edwin J. Henrie, MD

*Toussaint A. Leclercq, MD

Robert V. Lewis, MD

Robert Powel
Student

*Peter L. Mathieu, Jr., MD

*P. Joseph Pesare, MD

*Sumner Raphael, MD

Henry T. Randall, MD

*Guy A. Settipane, MD

*David T. Barrall, MD
Resident

*Member of Publications Committee

OFFICERS

Richard G. Bertini, MD
President

Boyd P. King, MD
President-Elect

William H. Colaiace, MD
Secretary

Frances P. Conklin, MD
Treasurer

Peter D.T. Clarisse, MD
Immediate Past President

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

DEC 24 1987

DISTRICT AND COUNTY PRESIDENTS

Charles J. Ashworth, Jr., MD
Bristol County Medical Society

Oswaldo R. Velis, MD
Kent County Medical Society

Edwin G. Singsen, MD
Newport County Medical Society

Martin Phillips, MD
Pawtucket Medical Association

Mary D. Lekas, MD
Providence Medical Association

Lyman A. Davenport, MD
Washington County Medical Society

Paul C. Hessler, III, MD
Woonsocket District Medical Society

Rhode Island Medical Journal is owned and published by the Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903, Ph: 401/331-3207. Single copies $2.00 — Subscriptions $15.00 per year (members of the Rhode Island Medical Society — $5.00 annually). Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Second class postage paid at Providence, Rhode Island and at additional mailing offices. **ISSN 0363-7913**

Added Control For America's Coughs

The expectorant action of guaifenesin plus the Advantage of Codeine!

Robitussin A-C®

Robitussin and codeine. Each 5 ml (*1 teaspoonful*) contains: Guaifenesin, USP, 100 mg; Codeine Phosphate, USP, 10 mg (*warning: may be habit forming*); alcohol, 3.5 percent; in a palatable, aromatic syrup

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

©A.H. Robins Company 1985

Volume 70, Number 12 December 1987

TABLE OF CONTENTS

527 **INDEX — VOLUME 70**

529 **EDITORIAL**

The Pawtucket Heart Health Program: A Community and a National Asset

H. Denman Scott, MD

531 **EDITOR'S MAILBOX**

CONTRIBUTIONS

533 **The Pawtucket Heart Health Program**

I. An Experiment in Population-Based Disease Prevention

Richard A. Carleton, MD
Thomas M. Lasater, PhD
AnnLouise Assaf, PhD
R. Craig Lefebvre, PhD
Sonja M. McKinlay, PhD

541 **The Pawtucket Heart Health Program**

II. Evaluation Strategies

Ann Louise R. Assaf, PhD
Stephen W. Banspach, PhD
Thomas M. Lasater, PhD
Sonja M. McKinlay, PhD
Richard A. Carleton, MD

549 **The Surgical History of Narragansett Bay**

A Dialogue with History

John J. Byrne, MD

Cover: *Photograph of the new Sayles Building, The Memorial Hospital, Pawtucket, Rhode Island. Courtesy of Louise Paiva, Public Relations, The Memorial Hospital.*

PHYSICIAN WANTED
TO COVER NIGHTS, WEEKENDS, AND HOLIDAYS
INSTITUTE OF MENTAL HEALTH

A 300-bed psychiatric hospital in Cranston is seeking physicians who are willing to work during off-hours to perform admissions of psychiatric patients and respond to medical and psychiatric emergencies. The duties are similar to those for a house medical officer.

The physician will work in collaboration with a qualified psychiatrist on administrative call.

70 hours/month
Salary: $300.00/night
Excellent sleeping quarters

Call the Medical Director at
464-2458

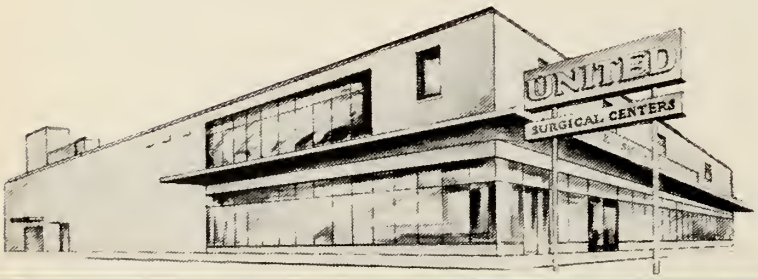
There must be a good reason why we've become the trusted back-up resource for more Rhode Island doctors (and their patients) than anyone else.

UNITED SURGICAL CENTERS
The Professionals in Home Health Care Equipment

We carry just about EVERYTHING for Home Health Care . . . which means, everything a patient or convalescent needs to implement the doctor's treatment directions. For Ostomy and Oxygen needs to Orthopedic Appliances, Wheelchairs, Walkers and Hospital Beds, we're here to serve your patients. Our staff is knowledgeable and dedicated to supplying exactly "what the doctor ordered". We've been doing it dependably for many years.

That's how we've earned the trust of so many doctors.

Medicare and Third Party Claims Accepted and Processed.



(401) 781-2166
OPEN DAILY 8 to 5:30 • SATURDAY 8 to 1

380 WARWICK AVE., WARWICK, RI 02888
At the Cranston/Warwick City Line

Rhode Island Medical Journal

Subject, Title and Author Index
Volume 70, 1987

SUBJECT INDEX

	Page
Adverse Drug Reaction	311
AIDS	
Blood Supply	11
Clinical Manifestations	19
Epidemic (editorial)	9
Epidemiology and Control	35
Obstetrical Team	441
Therapeutic Approaches	27
Blue Cross/Blue Shield (editorial)	161
Books Received	387, 511
Book Review	181
Cambodian Health Beliefs	73
Cancer	
Cancer Detection (editorial)	433
Control in Rhode Island	435
Colorectal Screening in Rhode Island	217
Catastrophic Coverage (editorial)	107
Certificate of Need	341
Chordomas	173
Continuing Medical Education Calendar	43, 317
CPR	487
Crohn's Disease (editorial)	483
Defense Committee Chairmanship	179
Disseminating Intravascular Coagulation	109
Doctor's Image	415
DRGs (editorial)	203
Elisha Bartlett	449
Female Urology	
Incontinence	293
Urinary Tract Infection	307
Have You Heard?	321, 377, 509
Headache (Recurrent)	163
Health Care 1986-87	79
HMOs	61
Holistic Health	205
Hospital Consortium (editorial)	59
Hunger	65
Hymenoptera Allergy	113
Long Term Care	213, 287
Medical-Legal Report Writing with Insanity as Defense	495
Neonatal Seizures	347
Pawtucket Heart Health Program	533, 541
Percutaneous Biopsy	127
Peripatetics	272, 375, 505
Presidential Address	355
Renal Failure with Anuria	501
RIMS	
Annual Address	409
Discourses	397, 401
Necrology 1986	239
175 Years (editorial)	395
Smoking	121, 162
Space Shuttle Tragedy	319
Sports Medicine	
Benefits and Risks of Physical Exercise (editorial)	237
Pediatric and Adolescent Knee Injuries	255
Rhode Island High School Athletic Injuries 1985-86	265
Upper Extremity Injuries	245
State Medical Journals (editorial)	203
Surgical History of Narragansett Bay	549
Young Persons' Health	361

CONTRIBUTION TITLE INDEX

	Page
A Five Year Review of Hymenoptera Allergy: 299 Patients	113
A Rhode Island Philosopher (Elisha Bartlett)	449
Acute Renal Failure With Anuria Caused by Aortic Thrombosis and Bilateral Renal Artery Occlusion. A Report of Two Cases	501
Acquired Immune Deficiency Syndrome (AIDS) and The Obstetrical Team	441
AIDS and the Blood Supply	11
The Annual Address (RIMS, June 13, 1912)	409
Cancer Control in Rhode Island, Part I. The Value of Screening for Cancer	435
Cautions to Young Persons Concerning Health	361
Certificate of Need: A State Perspective	341
The Challenge of Assessing and Treating Female Incontinence	293
Children and the Space Shuttle Tragedy	319
Chordomas: A Review	173
The Clinical Manifestations of the Acquired Immunodeficiency Syndrome	19
CPR: Ready or Not? A Rhode Island Perspective	487

Page

Diagnosis, Significance, and Treatment of Neonatal Seizures 347
A Discourse 397
Discourse on the Object and Utility of the Rhode Island Medical Society 401
Disseminating Intravascular Coagulation Following First Trimester Abortion in Polycythemia Vera 109
The Doctor's Image — Past, Present and Future 415
Dollars and Sense of Percutaneous Biopsy 127
The Epidemiology and Control of AIDS and HIV Infection in Rhode Island 35
Health Care 1986-87 79
Holistic Health: Implications for Physicians In a Changing World 205
How to Write a Medical-Legal Report for Litigation with Insanity as the Defense 495
Issues in the Management of Recurrent Headache 163
The Pawtucket Heart Health Program:
I. An Experiment in Population-Based Disease Prevention 533
II. Evaluation Strategies 541
Physician Screening Practices and Colorectal Cancer Screening Prevalence Among the Rhode Island Population 217
Presidential Address 355
Rhode Island High School Athletic Injuries 1985-86 265
Rhode Island Physician's Recognition and Reporting of Adverse Drug Reactions 311
Single Dose Therapy of Acute Urinary Tract Infection in Women Using Trimethoprim-Sulfamethoxazole: Experience in a Prepaid Internal Medicine Group Practice 307
Sixteen Years As Defense Committee Chairmanship 179
Some Thoughts on Long Term Care 213
Special Report — An HMO Experience 61
Sports Related Knee Injuries in the Pediatric and Adolescent Athlete 255
The Surgical History of Narragansett Bay 549
Therapeutic Approaches for AIDS and HIV Infection ... 27
Traditional Cambodian Health Beliefs and Practices 73
Understanding the Smoking Program and How to Help Patients Stop: Current Status of the Field 121
Upper Extremity Injuries in Athletes: An Overview 245
The World of Hunger 65

EDITORIAL TITLE INDEX

Page

The Aids Epidemic 9
The Benefits and Risks of Physical Exercise 237
Catastrophic Coverage A Delusion 107
Long-Term-Care Insurance 287
More On Tobacco 162
A New Tool for Cancer Detection? 433
A New Type of Hospital Consortium 59
175 Years Young 395
The Paradox of DRGs 203
The Pawtucket Heart Health Program A Community and a National Asset 529
Poetic Justice 483
State Medical Journals 339
The Trials of Blue Cross and Blue Shield 161

AUTHOR INDEX

Page

Abrams, David B. 121
Adelson, Samuel 415
Akelman, Edward 245
Andrews, Lisa G. 311
Apshaga, Susan 495
Aronson, Louise 73
Aronson, Stanley M. 9, 237
Assaf, AnnLouise 533, 541
Attanasio, Virginia 163
Austerlitz, Jeffrey 63
Banspach, Stephen W. 533, 541
Barcohana, Yussef 109, 441
Beitz, Jule G. 435
Byrne, John J. 549
Carleton, Richard A 533, 541
Chace, Barbara 307
Chamberlain, S.G. 113
Chazan, Joseph A. 501
Clarisse, Peter D. T. 355
Colt, Avery M. 311
Cooper, Shawn 319
Corkery, M. 341
Cronan, John J. 127, 501
Crowley, James P. 109
Cutler, Charles M. 64
Donahue, John X. 341
Dondero, L. 35
Dorfman, Gary S. 127
Endreny, Raymond G. 501
Esparza, Alfredo R. 127
Faich, Gerald A. 311
Fisher, Alvan E. 19
Fogel, Richard I. 501
Follick, Michael J. 163
Fowler, Joanne L. 163
Goldstein, Jonathan 487
Goldowsky, Seebert J. 59, 107, 161, 162, 203, 287, 339, 395, 433, 483
Herndon, James H. 265
Howard, B. A. 113
Johnson, A. 341
Jordan, Thomas A. 495
Juergens, John P. 311
Kaemmerlen, Susan 307
Kates, Robert W. 65
Keenlyside, Richard A. 35
Lance, M. Peter 217
Lasater, Thomas M. 533, 541
Lefebvre, R. Craig 533, 541
Lowe, Ernest B. Jr. 265
Manocchia, Augustine 487
Masterson-Allen, Susan 217
Mayer, Kenneth H. 27
McKinlay, Sonja M. 533, 541
Mor, Vincent 217
Mosher, Charles P. 73
Opal, Steven M. 27
Osler, William 449
Paolella, Landy P. 127
Perkins, Earle R. 265
Perry, Richard J. 163
Peters, Norman D. 173
Quevedo, Stephen F. 307
Rogers, Frederick T. 409
Rosenbaum, Sara E. 311
Sargent, Francis B. 179
Scott, H. Denman 341
Singer, Ira J. 255
Stewart, Ronald Mark 495
Sturner, William Q. 109
Susset, Jacques G. 293
Tierney, John T. 341
Trotter, Wayne 487
Waring, Edmund T. 397
Waterhouse, Benjamin 361
Waters, William J. 341
Weitberg, Alan B. 435
Wiecha, John M. 205
Williams, Donald C. 341
Yankee, Ronald A. 73
Zalneraitis, Edwin L. 347

Editorial

The Pawtucket Heart Health Program: A Community and a National Asset

The 1980s have not lacked medical success stories. Scientific advances have produced some startling results, but none more remarkable than the reduction in cardiovascular disease rates dating to the earliest landmark studies on community-wide intervention.

From 1968 to 1985, for example, deaths from ischemic heart disease in Rhode Island declined from 385.49 per 100,000 to 242.05, a dramatic 37 per cent. Even more dramatic, the death rate for cerebrovascular accidents dropped from 104.51 to 50.40 or 52 per cent.[1]

The Framingham (Massachusetts) Heart Disease Study begun in 1948 was crucial to our knowledge of the risk factors. It found that cigarette smokers, those with uncontrolled hypertension, and those with a high level of serum cholesterol in their blood were 10 times more likely to suffer a heart attack than persons in the control group. It found a direct correlation between a reduction in these risk factors and reduced coronary heart disease.

According to Whisnant, hypertension is the most important risk factor for stroke. Surveys have shown that in lowering blood pressure, antihypertensive medication was increasingly effective. Further clinical studies are needed, however, to examine the relationship between hypertension and cerebrovascular disease mortality.[2]

In the early 1970s, the Stanford Three-City Study in California and the North Karelia project in Finland attempted to alter the risk factors affecting cardiovascular disease by influencing them on a community-wide basis. These and other studies produced a promising increase in our understanding of behavioral change.

In the late 1970s, the Stanford Five-City Study and the Minnesota Heart Health Program further advanced our experience in this area.

From these beginnings our awareness of the importance of lifestyle changes in the prevention of disease has flowered into a major movement in the health-care industry.

Goldman and Cook estimated that 54 per cent of the decline in ischemic heart disease mortality in the United States between 1968 and 1976 was related to changes in lifestyle, specifically reductions in serum cholesterol and cigarette smoking. They attributed 40 per cent of the decline to specific medical interventions, the leading estimated contributors being coronary-care units and the medical treatment of ischemic heart disease.[3]

Public health advocates now seek to determine how best to influence positive lifestyle changes on a broad scale. The individual physician, while a vital factor in education and direction of his patients, is limited by the scope of his practice. Public health leaders hope to expand that function to entire communities.

Rhode Island is privileged to be the site of a world-renowned research project that in time may produce a compendium of answers to the goal of effective community-wide intervention. I refer, of course, to the Pawtucket Heart Health Program (PHHP) discussed at length in this and subsequent issues of the *Rhode Island Medical Journal.*

Started August 1, 1980 with Dr Richard A. Carleton, originator of the project, as principal

investigator, PHHP is funded by a grant from the National Heart, Lung and Blood Institute of the National Institutes of Health. Its research over the last seven years has attracted wide attention throughout the United States as well as in the Federal Republic of Germany, Wales, England, Canada, Sweden and the People's Republic of China.

PHHP is making significant contributions to the world's ability to induce behavioral change in entire populations — a process known as community activation. Public education efforts have focused on the serious risks of cigarette smoking, on dietary improvement, reducing high blood pressure, and enhancing overall physical fitness. Throughout, PHHP has sought and received the cooperation of numerous volunteers and the mass media, and employed various programs of direct health education including appropriate referral, risk-factor screening, and counseling.

It would be wrong to make community activation appear to be a simple procedure, implying that all a community has to do is to become involved in the health-education business and all problems will be solved. Unfortunately, it involves many variables and profound complexities. Individual motivation is strongly influenced by personal values and socio-economic characteristics, by cultural and regional factors. None of these can be ignored in designing behavioral and evaluation strategies.

The PHHP continues to serve as an inspiration to those of us in the public health field. Thanks to PHHP and its precursors, we will become increasingly skilled in reducing cardiovascular disease through community action. The corollary may be parallel efforts in the future to reduce the incidence of other diseases that have stubbornly resisted the best efforts of the medical-scientific community.

H. Denman Scott, MD
Director
Rhode Island Department of Health

References

[1] R.I. Department of Health, Rhode Island Plan for the Medical Management of Ischemic Heart Disease Through the 1990s. November 1987.
[2] Whisnant, J.P. The Decline of Stroke: Stroke, Jan.-Feb. 1984, 15(1):160-168.
[3] Goldman, L. and Cook, E.F. The Decline in Ischemic Heart Disease Mortality Rates: Annals of Internal Medicine, December 1984, 101:825-836.

EDITOR'S MAILBOX

More on Certificate of Need

To The Editor:
I am pleased that my paper "Certificate of Need: A Concept Whose Time Has Passed" in the *Rhode Island Medical Journal* of June 1986, elicited a response titled "Certificate of Need: A State Perspective" in the issue of August 1987. As expected, I do not agree with most of the concepts presented in that paper.

The amount of money claimed to have been saved by the certificate-of-need process is grossly exaggerated. Most proposals are purposely made much grander than needed as part of the process of negotiation. Further, the delays inherent in the process, which now takes almost one year, have resulted in cost increases due to the effects of inflation, which were much more important in the late 70's and early 80's.

The Rhode Island State Department of Health further states under benefits of certificate-of-need legislation: "Rhode Island has a relatively modest community hospital bed supply, 3.7 acute care beds per 1000 population versus 4.4 in the United States." Is this necessarily good when one considers the maldistribution of these hospital beds? Hospital beds in Providence and in Kent County are utilized at greater than 90% occupancy, while beds in northern Rhode Island frequently have occupancy as low as 50 to 60%. In addition, those of us who care for patients on a daily basis find it increasingly difficult to transfer patients from the most expensive facility, the acute hospital, to a nursing home bed. Do we really have enough nursing home beds? Did the certificate-of-need process, which rejected a number of these applications, do anyone a service?

It is also stated that "certificate of need brings issues to the forefront which require study." This is a euphemism for delay and prevention of individual or institutional initiative. Rhode Island was one of the last states to obtain CAT scanners. We have no organ transplantation programs and are one of only two states without magnetic resonance imaging (MRI) facilities. This latter problem will change soon, but in a highly structured and artificial way. The likelihood of any of the state-of-the-art or cutting-edge technology being developed or appearing early on in Rhode Island is extremely remote unless regulation is somewhat reduced.

The Health Department identified "the down side" and included delays in needed programs and the potential or overpoliticizing the Health issues." These are not risks, but realities. One has only to review the events of the past year to realize this: the cardiac catheterization problem, the Fatima Unit of St. Joseph Hospital Emergency Room, Roger Williams General Hospital Radiation and Cancer Center, the Miriam Hospital Ambulatory Center. Delay and politics are part and parcel of the year to-year certificate-of-need process.

The Health Department further points to three

major innovations in the certificate-of-need process: 1984 Concap, 1985 removal of HMO requests for proposal, and 1986 increases in certificate-of-need review thresholds. These are not progressive, but in fact retrogressive. The Concap, by combining all programs into one total dollar package, forces the choice between equally good, but unrelated programs, comparing apples with oranges. In a given year, worthwhile projects may exceed or fall short of the Cap, thus potentially excluding worthy projects or including less needed ones. The potential modifications represent much of the same bureaucracy and controls. If we do not learn from history, we are doomed to repeat the errors of the past.

It is not surprising that the Health Department supports the certificate of need. It is in the seat of power, controlling health expenditures throughout the state for many years. In partnership with the major health carrier and the legislature, they have been largely responsible for how health care has evolved over the past 20 years. This controlled, paternalistic approach has not necessarily been in the best interests of the citizens of Rhode Island.

The certificate of need cannot be blamed for all that has occurred, nor does it deserve undue credit for those things which have been accomplished. Rather the *concept of regulation* must be more carefully reviewed at a time when the health-care industry is undergoing revolutionary and convulsive changes. Now is the time to get some new players into the game and to reduce, not increase regulation. The Health Department states that "no one is particularily enamored by regulation; it is not a terribly uplifting experience." They might then relieve themselves of some of this activity and allow for more individual and institutional initiatives.

Joseph A. Chazan, MD
Division of Renal Diseases
Rhode Island Hospital
593 Eddy Street
Providence, RI 02903

LOCUM TENENS PHYSICIANS

Join a comprehensive physician support service with a major medical center in south central Montana.

Locum physicians provide primary care coverage (excl. routine OB) for physicians in rural Montana and Wyoming. Assignments vary in length. Reimbursement for expenses, malpractice, health insurance, CME.

Call Locum Tenens Coordinator
1-800-325-1774
Or send CV:
1500 Poly Drive, Suite 103
Billings, MT 59102

The Pawtucket Heart Health Program: I. An Experiment In Population-Based Disease Prevention

Richard A. Carleton, MD
Thomas M. Lasater, PhD
AnnLouise Assaf, PhD
R. Craig Lefebvre, PhD
Sonja M. McKinlay, PhD

Richard A. Carleton, MD is Principal Investigator for The Pawtucket Heart Health Program, Physician in Chief, Memorial Hospital, Pawtucket, Rhode Island, and Professor of Medicine, Department of Medicine, Brown University, Providence, Rhode Island.

Thomas M. Lasater, PhD is Project Director and Co-Principal Investigator for The Pawtucket Heart Health Program, and Associate Professor of Community Health, Brown University, Providence, Rhode Island.

AnnLouise Assaf, PhD is Evaluation Coordinator and Co-Investigator for The Pawtucket Heart Health Program, and Assistant Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

R. Craig Lefebvre, PhD is Intervention Coordinator and Co-Investigator of The Pawtucket Heart Health Program, and Assistant Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

Sonja M. McKinlay, PhD is Co-Principal Investigator for The Pawtucket Heart Health Program and Associate Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

Many chronic diseases afflicting modern society have been causally related to lifestyle choices. Obvious examples include disability from injuries related to a lack of seatbelt usage or motor cyclist helmets, the ravages of abuse of alcohol and other drugs, and the disease burden of lung cancer accruing to cigarette smokers. The scientific tale of causality in cardiovascular disease has been one encompassing much of the twentieth century. The first stage was the identification through studies such as the Framingham Heart Study, the studies in Tecumseh, Michigan, and many others of "risk factors for cardiovascular disease."[1] These studies have repeatedly demonstrated the incremental risk of heart attack and stroke associated with high blood pressure, with high circulating cholesterol levels, with smoking habits, and with other lifestyle attributes. The second major step in this scientific saga was the development and experimental testing of interventions designed to remove or attenuate elevated risk of cardiovascular disease. Statistical considerations led initially to experimental trials in high risk populations. Although some of these have been inconclusive,[2, 3] others have unequivocally demonstrated benefit of reducing markedly elevated cholesterol levels,[4] blood pressure,[5, 6] and cigarette smoking.[2] Experimental interventions to improve physical fitness or to control excess body weight with measurement of disease outcomes have not been conducted.

A third step in the scientific sequence has com-

prised interventions in individuals at lower risk than, for example, the upper 5 per cent of the population distribution of cholesterol studied in the Coronary Primary Prevention Trial of the Lipid Research Clinics.[4] Many of these studies have been completed, particularly with reference to blood pressure. Some have shown benefit comparable to those trials involving treatment of extreme blood pressure elevations.[5-7] Comparable studies of persons with lesser cholesterol elevations are currently being implemented.

Data from many studies, however, indicate that risk from elevated blood pressure and of elevated cholesterol is continuous and directly related to the degree of elevation. Large numbers of people have mildly elevated blood pressure, while only small numbers have markedly elevated blood pressure. This fact implies that blood pressure control across an entire population should result in substantial reductions in cardiovascular disease. Similarly, the attributable risk from the large number of people with mildly increased cholesterol levels is large. From this perspective, it seemed rational to contemplate experimental intervention targeting an entire population — those at high risk, those at low risk and, indeed, an entire community. An additional rationale exists for an experiment to test community-based intervention as a means of reducing cardiovascular disease. Human behaviors such as those concerning foods habitually consumed, the practices that lead to improved blood pressure control, the decision not to smoke cigarettes, the decision not to control excess weight, and the decision to remain physically fit are all influenced by both individual factors and social factors. Individual, family, organizational, ethnic, cultural, and community expectations all influence individual behavioral choices important in the control of each of the behaviorally influenced cardiovascular risk factors. Intervention targeting only individuals should, one may postulate, be less effective than intervention reaching all elements of a society found in an intact community.

It was with this scientific background and this perspective on the complexities of human behavior that the Pawtucket Heart Health Program (PHHP) was born. A research grant project, the PHHP has received repeated successful peer review by representatives of the National Heart, Lung and Blood Institute of the National Institutes of Health. The project bears scientific similarities to other pioneering work.[8, 9]

This paper will present an overview of The Pawtucket Heart Health Program, briefly describing the experimental design, the conceptual approach to population-based behavior change, the sophisticated scientific evaluation strategies utilized, and hypotheses concerning anticipated outcomes. Other papers in this symposium will address issues of application of social marketing principles to the community-based behavior change process, illustrative examples of approaches to influencing behavior of citizens of an entire community, and approaches to evaluation.

This is the first of a series of five papers describing the structure and goals of The Pawtucket Heart Health Program. The second paper follows in this issue of the JOURNAL. Others will appear in subsequent issues.

Pawtucket Heart Health Program Research Model

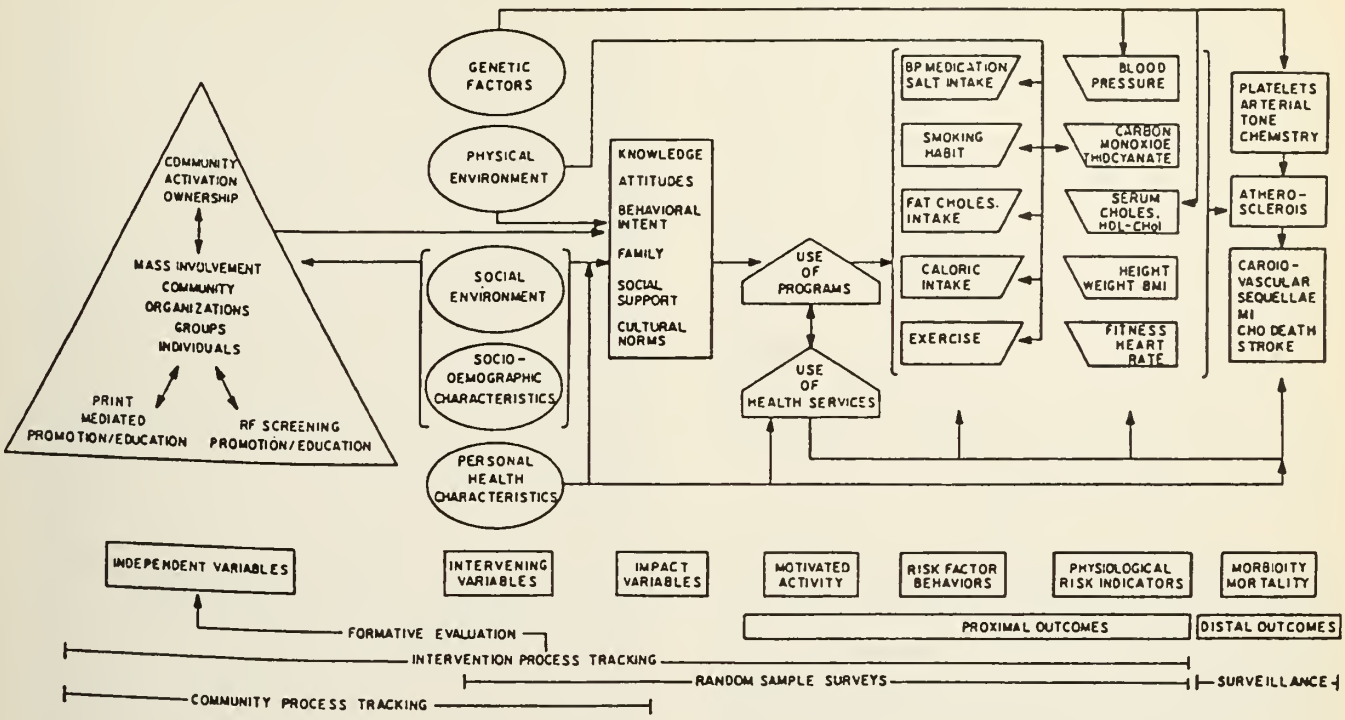
The PHHP research model is presented in Figure 1. As with any experiment, an independent variable is applied to the scientific system. In this instance, the independent variable is an elaborate process of community involvement in the behavior change process — a process called community activation. For this purpose, access to the public is achieved by focusing particularly upon program delivery by volunteer peers, through the media, through direct health education and through risk-factor screening, counseling, and appropriate referral programs.

The last critical component of any experimental design are those events here labeled distal outcomes. Distal outcomes in the PHHP are those diseases directly attributable to the atherosclerotic process. Between the independent variable and the dependent variable in any experiment

From the Department of Medicine, Memorial Hospital of Rhode Island, Pawtucket, Rhode Island and the Department of Medicine, Brown University, Providence, Rhode Island; the Division of Health Education, Memorial Hospital of Rhode Island, Pawtucket, Rhode Island; the Department of Community Health, Brown University Program in Medicine, Providence, Rhode Island; and the New England Research Institute, Waltham, Massachusetts.

Supported, in part, by Grant HL23629 from the National Heart, Lung, and Blood Institute, United States Department of Health and Human Services.

Fig 1: Pawtucket Heart Health Program Research Model



lies an often complex array of other factors important to the experimental design. Many of these are illustrated in Figure 1. The risk factors themselves are physiologic or pathophysiologic attributes such as cholesterol level, blood pressure, and physical fitness. Each of these, in turn, is influenced by specific personal behaviors. It is postulated that these, in turn, are influenced by recruiting citizens into special programs designed to change that behavior. Many personal characteristics and socio-economic characteristics existing in the community influence the motivation for and pursuit of these activities. Finally, many intervening variables also influence program impact.

Figure 1 also illustrates the diversity of evaluation strategies used by PHHP. Careful morbidity and mortality surveillance provides measurement of distal outcomes in the form of population rates of myocardial infarction and stroke, and disease-specific death rates. Whether people use programs, how they behave, and the prevalence or intensity, or both of the diverse cardiovascular risk factors are measured by random sample surveys of the populations of each city. The intervention activities themselves are a complex amalgam of educational, behavioral, and social science-based processes. To insure that these are effective and properly applied requires a unique formative and process evaluation system through which the intervention process is carefully tracked. To this end, computer tracking files of participants and events are maintained. In turn, effectiveness of each program component can be continuously enhanced through a process of formative feedback to improve program access and influence. Moreover, the intensity of intervention, or the "dose" of treatment given the population can be measured. Lastly, any experimental design must be cognizant of and protect against faulty interpretation. One major bias which might confound interpretation would be naturally-occurring time trends independent of the intervention program. For this reason, in community-based research, as in other research, a control population is critical.

Experimental Design

Random allocation of communities to intervention and control groups, while theoretically highly desirable, proved practically to be impossible. Accordingly, a careful rational process of selection of an intervention community and, separately, of a control community was carried out early in the design of the Pawtucket Heart Health Program. Census data, as updated through 1975, were used to identify two communities containing between 40,000 and 100,000 people with the requisite sta-

bility of in-migration and out-migration necessary for long-term follow up. These two communities were then matched carefully for sociodemographic variables. The intervention community chosen was Pawtucket, Rhode Island, a predominantly blue-collar community of 71,204 citizens. A comparable comparison community in New England was also chosen. Both communities underwent baseline random sample surveys. The results demonstrated remarkably similar levels of cardiovascular risk factors in the populations of each city.

This quasi-experimental design has both strengths and limitations. A major strength is the opportunity to detect secular trends in cardiovascular morbidity and mortality in a population initially very similar to that of Pawtucket.

Scientific Hypothesis

The research laboratories were then set. The experimental design had been established. The many elements important in such a complex experiment had been arrayed in a suitable research model. Funding from the National Heart, Lung, and Blood Institute began on August 1, 1980. Recruitment of a talented multi-disciplinary scientific staff was begun and completed. The project was then ready to begin testing a sequence of scientifically linked hypothesis:

- A self-help approach to community health change, using predominantly volunteer lay facilitators is feasible;
- a community activation community ownership program will produce wide-spread involvement by individuals, groups, and organizations and by the entire community to produce a health promotive cultural change process;
- development of health promotive social support networks will result in increased knowledge concerning risk factors, facilitate risk factor related behavior change, and aid in maintenance of those changes;
- corresponding changes will occur in physiologic risk factors measured in successive random samples of the Pawtucket population;
- the changes in physiologic variables will later be manifest as reduction in atherosclerosis-related morbidity and mortality from coronary heart disease and stroke; and
- these changes in knowledge, in behavior, in psychologic variables, in morbidity, and in mortality will occur to a greater extent in Pawtucket than in a demographically similar reference city or in other comparable reference populations.

Pawtucket Heart Health Program Sequence

The Pawtucket Heart Health Program initially established a theoretical framework for population-based behavior change. Stemming from social-learning theory and other behavioral change principles, factors relevant to behavioral community psychology, to social marketing, and to many other disciplines were brought to bear on the intervention process. Recognition of the complex network of relationships in which each individual lives provided an additional dimension to the intervention plans of PHHP. Accordingly, multiple programs targeting each of the five dominant cardiovascular risk factors were developed. Each focused on means of promoting the program and of augmenting motivation for change, on teaching of skills necessary to achieve new behaviors, on teaching of skills through which an individual could build a social support system for the new behaviors, and on providing insights for individual and collective strategies for maintaining new behaviors throughout the community. A third dimension of the complex intervention project concerned developing programs to influence individuals, groups of individuals, entire organizations, and ultimately the entire community.

A calendar of events of PHHP activities is presented in Figure 2. An initial planning phase was carried out during the first random sample survey (XS-1) of the population in Pawtucket and in the comparison city. Sample sizes sufficient to insure statistical significance were established, as were specific, reproduceable, cost-effective, and valid survey procedures. Hospital-record-based surveillance for all fatal or nonfatal myocardial infarctions and strokes was begun.

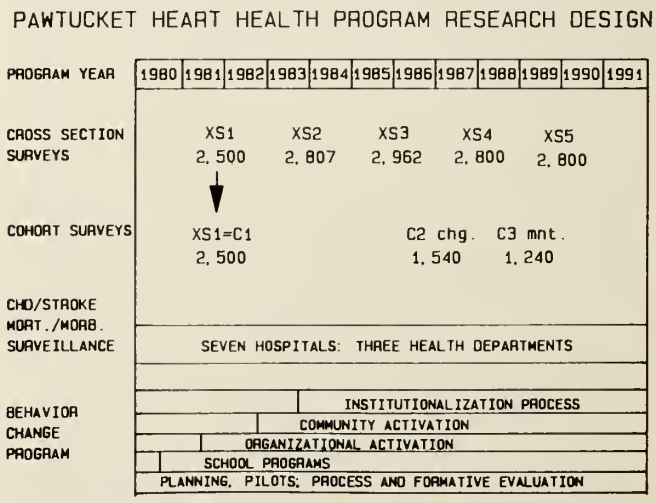


Fig 2: Pawtucket Heart Health Program Timetable

Repeated risk factor surveys to assess change over a period of time were conducted on a biennial basis. The survey participants examined in 1981-82 were re-examined in 1986-87 (CS-1) and will be examined once again (CS-2).

The Formative and Process evaluation system, through which program element effectiveness is assessed, was developed and implemented. School-based programs were begun. Diverse organizations, such as worksites, churches, social clubs, grocery stores, and restaurants began their involvement with appropriate activities. Increasingly, agencies such as the Parks and Recreation Department of the City of Pawtucket have adopted portions of the program and have maintained them over the years. This process of institutionalization promises long-term program maintenance beyond the duration of research funding.

The research effort has been subjected to repeated review by the scientific community. Augmented funding was provided in 1986 designed to carry the intervention program intervention into 1990. Disease-outcome surveillance will continue through 1991 at a minimum. The potential for even greater subsequent effects on disease makes a continuing surveillance system scientifically attractive.

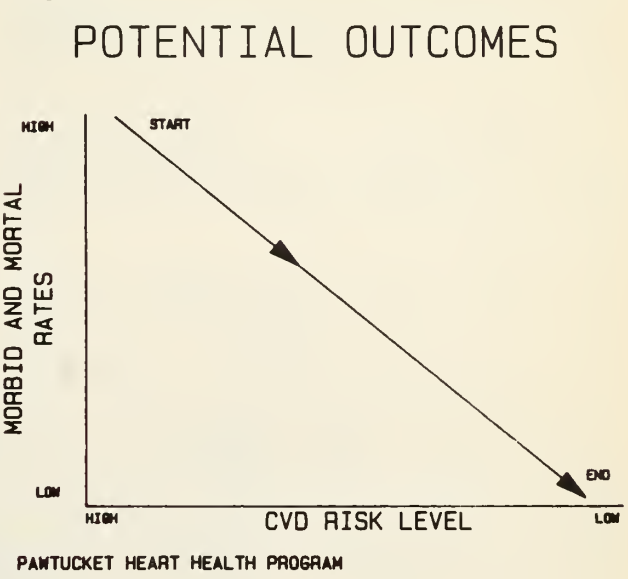
Outcomes

A number of goals have been set for The Pawtucket Heart Health Program. The overarching scientific question being addressed is whether it is possible to influence an entire population such that they behave differently, achieve lowered cardiovascular risk, and experience less disabling or lethal cardiovascular disease. The magnitude of these effects cannot be predicted with precision at this time. The Pawtucket Heart Health Program is designed to produce the statistically significant outcomes listed:

- 6 per cent reduction in average total cholesterol;
- 6 mmHg reduction in average systolic blood pressure;
- 30 per cent reduction in the proportion of active smokers;
- 2 per cent reduction in body weight and body mass index;
- 2 ml/kg/min increase in estimated maximal oxygen uptake; and
- 15 per cent reduction in total(fatal and non-fatal) cardiovascular disease event rates.

The results of The Pawtucket Heart Health Program cannot be predicted with accuracy. Uncertainty of outcome is inherent in the scientific experimental process. The sequential hypotheses presented previously, however, predict an outcome of the sort illustrated in Figure 3. Cardiovascular risk factors will decline significantly in Pawtucket. Smaller, but parallel trends will probably occur in the comparison community as part of national secular trends in several cardiovascular risk factors. As a sequel of reduced risk in Pawtucket, and following a lag that is not yet well characterized, cardiovascular mortality and morbidity will be substantially reduced in Pawtucket — substantially more than in the comparison city.

Fig 3: Potential Outcome of the Pawtucket Heart Health Program



Summary

The Pawtucket Heart Health Program is a population-based experiment designed to test whether behavioral strategies applied to an entire population can result in health promotive behaviors, in reduced burdens of premature disease, and in longer healthy lives. This project and the associated health promotive activities in the State of Rhode Island will continue to be watched closely by scientists throughout the nation and the world.

Acknowledgement

We are grateful to the many talented and dedicated staff, present and past, of the Pawtucket Heart Health Program for making the program possible.

References

1. The Pooling Project Research Group. Relationship of Blood Pressure, Serum Cholesterol, Smoking Habit, Relative Weight, and ECG Abnormalities to Incidence of Major Coronary Events: Final Report of the Pooling Project. Journal of Chronic Diseases, 31:201, 1979.
2. Multiple Risk Factor Intervention Trial Research Group: Risk Factor Changes and Mortality Results. JAMA 248:1465, 1982.
3. Rose G., Tunstall-Pedoe H.D., Heller R.F.: UK heart disease prevention project: incidence and mortality results. Lancet 1:1062, 1983.
4. The Lipid Research Clinic Coronary Primary Prevention Trial Results, JAMA 251:351, 1984.
5. Hypertension Detection and Follow-up Program Cooperative Group. Five-year findings of the Hypertension Detection and Follow-up Program: I Reduction in mortality of persons with high blood pressure including mild hypertension. JAMA 242:2562, 1979.
6. Veterans Administration Cooperative Study Group on an Anti-Hypertensive Agents: Effects of Treatment of Morbidity and Hypertension. II Results in Patients with diastolic blood pressure average 90 through 114mmHg. JAMA 213:1143, 1970.
7. Management Committee of the Australian Therapeutic Trial in mild hypertension. The Australian Therapeutic Trial in Mild Hypertension. Lancet 1:1261.
8. Farguhar J., Maccoby N., Wood P., Breitrose H., Haskell W., Meyer A., Alexander J., Brown W., McAlister A., Nash J., and Stern M. Community Education for Cardiovascular Health. Lancet, 1:1192, 1977.
9. Ehnholm C., Huttmann J., Pietinan P., Leino V. Mutanan M., Kostianen E., Pikkarainen J., Dougherty R., Iacono J., and Puska P. Effect of Diet on Serum Lipoproteins in a Population with a High Risk of Coronary Heart Disease. New England Journal of Medicine, 307:850, 1982.

DOCTORS WANTED

Like the Marines, we are also looking for a few good men (or women). However, we seek Board Certified Physicians, who are particularly proficient in patient history and physical examinations.

Medical Assessment Programs, with medical facilities in Boston and Springfield, Mass., and in Providence, R.I., provides comprehensive independent medical examinations for Workers' Compensation, Liability and Bodily Injury patients.

Full and Part-time positions available. Hours are Monday through Friday 9 to 5. No nights and no weekends.

Excellent benefits and salary.

Call Dr. Smith at (617) 449-8201.

Medical Assessment Programs
32 Fremont St.
Needham Heights, MA 02194

THE MAIN ARTERY

"Rhode Island's Heart Health Resource Center"

The Main Artery offers walk-in total blood cholesterol measurements, diet assessment and blood pressure checks. Also available are books on nutrition, smoking, diet, cholesterol, fitness and blood pressure; all reviewed and recommended by qualified risk factor professionals. Self Help Kits, encompassing all risk factors, may also be purchased.

The Main Artery is open Monday through Friday from 9 am to 4:30 pm, Thursdays until 6 pm and Saturdays 9 am to 1 pm. Cholesterol screenings are Tuesday, Thursday and Saturday, only.

The Main Artery, located at 260 Main Street in downtown Pawtucket, is a cooperative effort of the Memorial Hospital of RI and the Pawtucket Heart Health Program.

Call 722-PHHP for more information.

The True Test Of An Investment Management Team Is Its Ability To Pull Together, With Separate Strengths.

Today, managing your financial assets demands a concerted team effort. And the capacity to respond to changes in the economic climate, while still focusing on your individual goals.

The Hospital Trust Investment Management and Trust Group is uniquely qualified to provide this combination of strengths.

Indeed, you'd have to hire specialists in stocks, bonds, real estate, precious metals and international investments to rival the diversity we offer under one roof.

Discover how you can harness this strength to reach your financial goals. For a uniquely objective evaluation of your investment needs or more information, call Gary Gherardini, Vice President, at 278-8730.

Hospital Trust

a BANK OF BOSTON company

INVESTMENT MANAGEMENT AND TRUST GROUP

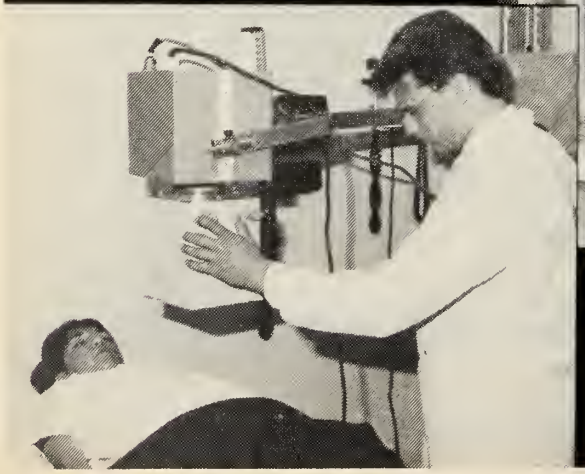
We've become the largest full service medical lab in Rhode Island...*because:*

- ✔ We are Licensed nationally by the Center for Disease Control (CDC), and participating members of the American Association of Bioanalysts (AAB) and the American Association of Medical Technologists (AAMT).
- ✔ A board certified pathologist, as a member of our staff, oversees the work of all our trained lab technicians.
- ✔ Our eight patient service centers, strategically located throughout the State, offer the fastest, most convenient and widest range of in-house testing facilities in Rhode Island. Our trained couriers pick up specimens and hand-deliver reports. Our lab supervisors are always available to discuss testing procedures and results.
- ✔ We offer many special services, such as Pathology, Mobile X-ray, EKG and Holter Monitoring. We even offer a 24-hour stat service every day of the year.

CML

CALL 943-1211

R.I. TOLL FREE 1-800-942-1011



CRANSTON MEDICAL LABORATORY, Inc.

WEST BAY MEDICAL CENTER, 1370 Cranston Street, Cranston, RI 02920

SERVICE CENTERS: Cranston • Pawtucket • Coventry
Narragansett • West Warwick • Cumberland

The Pawtucket Heart Health Program: II. Evaluation Strategies

AnnLouise R. Assaf, PhD
Stephen W. Banspach, PhD
Thomas M. Lasater, PhD
Sonja M. McKinlay, PhD
Richard A. Carleton, MD

AnnLouise R. Assaf, PhD is Evaluation Coordinator and Co-Investigator for The Pawtucket Heart Health Program, and Assistant Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

Stephen W. Banspach, PhD is Formative and Process Field Supervisor for The Pawtucket Heart Health Program, and Assistant Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

Thomas M. Lasater, PhD is Project Director and Co-Principal Investigator for The Pawtucket Heart Health Program, and Associate Professor of Community Health, Brown University, Providence, Rhode Island.

Sonja M. McKinlay, PhD is Co-Principal Investigator for The Pawtucket Heart Health Program and Associate Professor with the Department of Community Health, Brown University, Providence, Rhode Island.

Richard A. Carleton, MD is Principal Investigator for The Pawtucket Heart Health Program, Physician in Chief, Memorial Hospital, Pawtucket, Rhode Island, and Professor of Medicine, Department of Medicine, Brown University, Providence, Rhode Island.

We have hypothesized that the Pawtucket Heart Health Program (PHHP) will have a major impact on the behavioral practices, on the cultural norms, and on the cardiovascular risk of the community.[1] Over time our extensive evaluation efforts will tell us the validity of these hypotheses. As a research and demonstration project, we are committed to in-depth evaluation of all of our intervention strategies, and of the distal outcomes described previously.[1] This evaluation effort requires over 60 per cent of the project budget and about 45 staff members.

The Evaluation Unit of the Pawtucket Heart Program employs several different measurement strategies including biennial random household risk factor surveys, a morbidity and a mortality surveillance system, and formative and process evaluation. This paper will describe briefly the survey and surveillance efforts and will then focus on the formative and process evaluation techniques developed at PHHP.

In the PHHP research design and timeline, five cross-sectional household surveys of approximately 2,800 individuals per survey are planned. We have recently begun our fourth health survey anticipating approximately 1,400 completed interviews in each city. Participants in the first survey have been re-examined during the past year and will be re-examined once again to provide the increased sensitivity to detect change provided by repeated cohort surveys.

Two cities were selected in the quasi-experi-

Table 1. Summary of 1980 Census Data for Pawtucket and a Comparison City

	Pawtucket	Comparison City
Gender and Age		
Males — Median Age	31.3 yrs.	30.4 yrs.
Females — Median Age	36.6 yrs.	36.0 yrs.
Race and Ethnicity:		
% White	95.3	89.3
% Black	1.4	2.7
% Other	3.3	8.0
% Foreign Born	15.8	23.8
% of Foreign Born from Selected Countries		
United Kingdom	9.0	2.6
Italy	2.8	0.6
Portugal	36.8	64.0
Other Europe	16.1	15.9
Canada	9.4	4.0
% Age 5+ Who Speak a Language Other than English at Home	24.7	40.6
Household Characteristics:		
Persons per Household	2.5	2.5
% Population in Group Quarters	0.9	1.9
% Individuals Living Alone	29.4	26.8
% Families with Female Householder, no Husband Present, with Own Children Under 18 Years	10.0	6.3
Marital Status: (Population Age 14+)		
Male		
% Single	30.2	29.2
% Married, incl. Separated	60.5	62.4
Female		
% Single	24.8	23.0
% Married, incl. Separated	52.0	52.9
% Widowed	16.1	16.7
Education:		
Population Age 25+		
Median School Years Completed	11.9	9.5
% High School Graduates	49.8	38.1
Male	52.0	37.0
Female	48.0	37.0
% College Graduates	8.6	6.2

mental design. Both are in New England. Comparative data concerning Pawtucket and the comparison community are shown in Table 1.

As shown in Table 2, the two communities were also very similar with respect to the major cardiovascular disease risk factors, based on the initial random sample survey.

PHHP Survey

The PHHP Survey maintains a separate identity to assure cross-city comparability. Households are randomly selected from the Polk Directory in Pawtucket and from city street lists in the comparison city. These lists were updated before the first survey by a block supplement sample as described by Kish.[2] Within each sampled households, a single respondent is selected from the eligible adults (aged 18 through 64 years at last birthday), using selection tables adapted from those proposed by Kish[2] and by Deming[3] to approximate a random selection process.[4]

The PHHP household interview and testing protocol is administered in the home of respondents in English, Portuguese, or Spanish. The interview and examination lasts approximately 35 minutes. Questions about diet, exercise, smoking, behavior, and knowledge of cardiovascular disease are asked in addition to basic sociodemographic questions. Physiological measures include height, weight, blood pressure, total cholesterol, triglycerides, high-density-lipoprotein-bound cholesterol and serum cotinine.[5] A subsample of the respondents is selected as subjects for an in-home step test to estimate maximum oxygen uptake as a measure of fitness.[6] A second sub-sample is selected for completion of the Wil-

Table 2. Risk Factor Cross Sectional Survey I Data From Pawtucket and a Comparison City

	Pawtucket Male/Female	Comparison City Male/Female
Age 18-24		
% Smokers	42/48	44/152
Systolic Blood Pressure	122/111	123/113
Diastolic Blood Pressure	73/69	72/69
Cholesterol	170/171	173/173
HDL	46/54	46/51
Body Mass Index	24/22	25/24
Age 25-44		
% Smokers	46/43	52/40
Systolic Blood Pressure	126/115	125/115
Diastolic Blood Pressure	79/72	77/73
Cholesterol	202/187	206/194
HDL	44/57	46/52
Body Mass Index	27/25	26/26
Age 45-64		
% Smokers	49/31	39/26
Systolic Blood Pressure	137/133	138/133
Diastolic Blood Pressure	84/81	85/81
Cholesterol	225/236	231/233
HDL	44/56	46/58
Body Mass Index	27/27	28/28

lett diet questionnaire[7] to assess dietary habits. Stringent reliability and validity studies are routinely performed on physiological measurements.

Reports of these physiologic measurements are sent to each respondent and to his or her private physician if so desired.

The data management staff of the project performs many functions including providing a very responsive tracking system for survey management. This tracking system is used to select 10 per cent of all survey interviews for quality control by the field supervisors. The household-survey response rate, defined as the number of completed field protocols divided by the number of eligible households, has been about 70 per cent for all three surveys completed thus far, assuring a high degree of statistical power to detect changes.

Morbidity and Mortality Surveillance

The critical outcome of the Pawtucket Heart Health Program is the rate of cardiovascular disease. Both communities are screened for morbidity and case-fatality rates for coronary disease and stroke. To meet this goal, we have developed a reliable, cost-effective method of hospital record abstraction and electrocardiographic recoding for all pertinent hospital discharges.[8] Similar approaches have been designed for out of hospital deaths and for stroke endpoints.

The PHHP is one of three similar projects in the nation.[9, 10] Outcome criteria have been developed collaboratively by the three, with supplemental funding by the National Heart, Lung, and Blood Institute, to maximize the scientific value of the conclusions drawn by the three studies, and to allow pooling of final data. An epidemiological approach to diagnosis, rather than a clinical approach was adopted for surveillance, keeping in mind a goal of 100 per cent sensitivity and specificity. Because PHHP surveillance will span an 11-year period, it was necessary to design an epidemiologic algorithm for identification of cardiovascular events which was based on definitions and criteria least likely to be affected by charges in technology or clinical practice. Without the constraints of the clinical situation, the epidemiologic surveillance system was designed to minimize the rate of false positives. Objective data from the medical record rather than subjective data are used. Record abstractors, after intensive training and certification using "gold standard" records, are subject to stringent quality control. Each abstractor is also required to sign an oath of confidentiality. The diagnostic algorithm which is computerized requires no abstractor interpretation. The computer selects one of the three final diagnoses — definite event, possible event, or non-event based upon the algorithm in most cases. A minority require electrocardiagraphic coding[10] to supplement the enzyme-driven algorithm.

Out-of-hospital deaths are reviewed and coded in a similar manner with information obtained from an informative interview administered over the telephone.

Formative and Process Evaluation

To change distal outcomes requires a sequential series of steps, as has been described in the companion paper.[1] The present paper will now describe an important component of the evaluation of the intervention program, the Formative and Process evaluation system.

The Formative and Process evaluation system is a powerful and unique system developed at PHHP to serve two overarching purposes: (a) to increase the sensitivity to detect major confounding factors related to either local or national events; and (b) to examine in detail the implementation of the intervention and its short-term impact on the experimental community.[11, 12] These two purposes translate into two major functions: (a) community process tracking; and

(b) intervention process tracking.

Community Process Tracking provides continuing assessment of intervening variables such as quality of health care, social support networks, programmatic environment, and information environment. It also tracks impacting variables and the utilization of new or existing programs in the community. Community Process Tracking is accomplished by maintaining annual interviews with informants in key health related agencies in both cities by personal interviews with the agency manager or program director. The interviews are standardized and include information concerning the agency's primary misson, the agency's reach, health promotion topics covered by the agency, chronology of health-promotion activities conducted in the community and relevant programs planned for the immediate future. Newspaper content is also analyzed from the daily newspapers in both cities to provide a catalogue and count of health-related articles and cigarette advertisements. In Pawtucket, articles and announcements are subdivided into those initially by PHHP, those referring to PHHP, those of general health-promotion interest, and those mentioning cardiovascular disease risk factors.

Intervention Process Tracking, the second major function, fulfills four major purposes: documentation of intervention "dose," refinement of intervention programs, assessment of short term impact of PHHP programs, and provision of an historical record of the intervention. The process-tracking system yields systematic records of the intervention process. Documentation of PHHP activities is obtained at all four of the relevant levels of social structure targeted by the intervention program: community, organizations, groups, and individuals.

This documentation of intervention activities is accomplished through a system of tracking files. One file is the Program Tracking File. This file, designed to track program activities involving community-wide events, specific organizations, and groups, includes information on each program, such as materials used, types of activities, time, location, and attendance both of the group leaders and of the individuals participating in the program. Indices of intervention activities are abstracted from these files on a monthly basis and shared with the Intervention Unit staff.

The second file is the Volunteer File, which tracks volunteer participation by effort expended and type of activity. Each volunteer for PHHP completes a questionnaire including sociodemographic characteristics, reasons for volunteering, personal health history with particular emphasis on coronary disease and risk factors, availability, and an inventory of past experiences and skills relevant to the project. In addition, a monthly log is maintained on each volunteer including major tasks and amount of time spent on each item. Finally, face-to-face interviews are conducted with samples of those volunteers who resign, of those who are particularly successful, and of some of those filling each of the types of volunteer roles.

The Contact Card File is the largest tracking file. The contact cards, which are distributed and collected by the intervention staff and volunteers, collect basic sociodemographic and social-network data on each participant. These cards are completed by every individual who enrolls in a behavior change program. They serve as a sampling frame for selecting individuals, by PHHP activity, for a telephone survey. The telephone survey gathers additional sociodemographic information on participants, as well as information on cardiovascular-risk-factor status, behavior, and knowledge.

The telephone survey questionnaire is administered to samples of participants within 4-6 weeks of their joining a PHHP activity. Some of these same questions are then asked in follow-up interviews 6 and 12 months later of a portion of the initial sample. This survey design provides estimates of the immediate and intermediate term change in risk factor status and behavior of PHHP participants efficiently and at low cost with a response rate of over 90 per cent.

Many of the topics investigated in the telephone survey were purposely designed to be equivalent to those covered in the cross-sectional Health Survey. Both surveys collect data on risk factor status — the Health Survey by physiological and self-report measurements and the Telephone Survey by self-report only. This comparability increases the breadth of the data collection effort so that information is collected simultaneously on both the general community and the program participants. Continuing comparisons between participants who join PHHP and all citizens of both the education and comparison communities can then be made. All information is handled in confidence by using a unique identifier for each person. By assigning a systematic identification (ID) number to each PHHP activity, the Contact Card information can be entered into a hierarchical computer file which enables examination by individual and by activity. This computer file allows monitoring of the "dose" of

the intervention that each individual and the entire city receives. Participants can also be traced throughout the history of their involvement with PHHP by activity and dates of involvement. This system also allows for tracking specific subsets of the population and provides an opportunity to measure generalization across risk factors and activities.

These data also permit the intervention personnel to refine programs. This use of process data for formative purposes is a continuing process. Effective programs can be improved; ineffective programs can be changed or eliminated.

Finally, graphic displays of the type shown in Figures 1 and 2 are periodically posted to provide a large intervention staff with regular updates on their diverse activities and the immediate outcomes of their organizational efforts. Such use of Formative and Process tracking data allows the intervention staff to adjust programs better to reach their target populations.

The evaluation activities of the Pawtucket Heart Health Program are diverse, scientifically based, and provide both the short-term and long-term measures by which the research hypotheses will be tested.

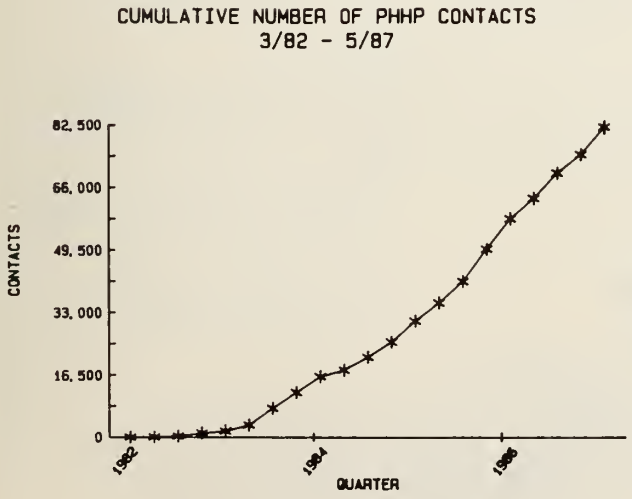
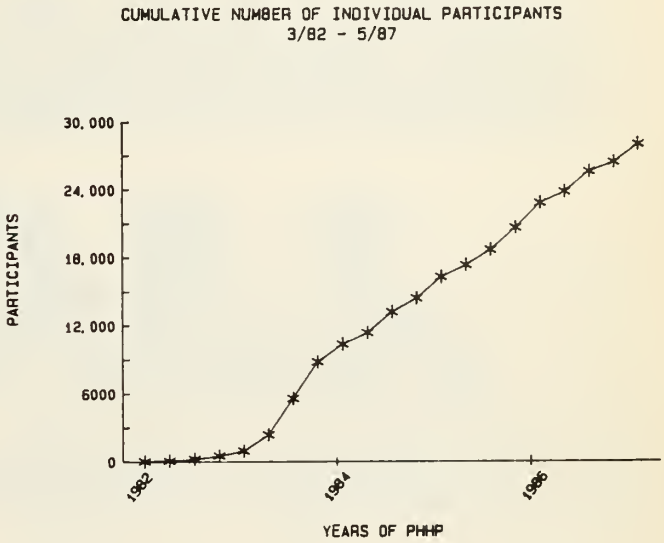


Fig 1: Cumulative Number of Contacts by Participants in Pawtucket Heart Health Program Activities

Fig 2: Cumulative Number of Unique Individuals Who Have Been Active Pawtucket Heart Health Program Participants.



Acknowledgements

Special thanks are extended to members of the Evaluation Unit of PHHP without whom this work would not have been possible. In particular, recognition to Ms. Joyce McKenney, Field Supervisor, for her dedication and contribution to this work.

References

[1] Carleton RA, Lasater TM, Assaf AR, Lefebvre RC, McKinlay SM: The Pawtucket Heart Health Program: An experiment in population-based disease prevention. Rhode Island Medical Journal 70:(12): 1987, pp. 533-538.

[2] Kish L: Survey sampling, New York, 1965, Wiley and Sons.

[3] Deming WE: Sample design in business research, New York, 1960, Wiley and Sons.

[4] McKinlay SM, Kipp DM, Johnson P, Downey K, Carleton RA: A field approach for obtaining physiological measures in surveys of general populations: response rates, reliability, and costs. Health Survey Research Methods: Proceedings of the Fourth Conference on Health Survey Research Methods, Washington, DC, 1982. DHHS Pub. No. (PHS) 84-3346, 1984.

[5] Kipp D, et al: Health Survey field manual, 3rd edition, November 1983.

[6] Siconolfi SF, Garber CE, Lasater TM, Carleton RA: A simple, valid step for estimating maximal oxygen uptake in epidemiologic studies. American Journal of Epidemiology 121(3):382-390, 1985.

[7] Willett W, et al: Reproducibility and validity of a semi quantitative food frequency questionnaire. American Journal of Epidemiology 122(1):51-65.

[8] McKinlay SM, Carleton RA, McKenney JL, Assaf AR: A new approach to surveillance for myocardial infarction: reproducibility and cost efficiency. (In submission), 1987.

[9] Mascioli SR, Jacobs DR, Kottke TE: Diagnostic criteria for hospitalized acute myocardial infarction: The Minnesota experience. (In submission), 1987.
[10] Fortmann SP: A comparison of methods for community surveillance of myocardial infarction rates. (In submission, 1987).
[11] McKinlay SM, McGraw SA, Assaf AR, Kipp DM, Carleton RA: An innovative approach to the evaluation of large community programs. (In submission), Academic Press, 1987.
[12] McGraw SA, et al: Methods in program evaluation: The formative and process evaluation system of the Pawtucket Heart Health Program. (In submission), 1987.

From the Department of Medicine, Memorial Hospital of Rhode Island, Pawtucket, Rhode Island and the Department of Medicine, Brown University, Providence, Rhode Island; the Division of Health Education, Memorial Hospital of Rhode Island, Pawtucket, Rhode Island; the Department of Community Health, Brown University Program in Medicine, Providence, Rhode Island; and the New England Research Institute, Waltham, Massachusetts.

Supported in part, by Grant HL23629 from the National Heart, Lung, and Blood Institute, United States Department of Health and Human Services.

Seeking referrals for

Multiple Clinical Studies

Clinical Programs Ltd. is now testing new psychiatric drugs for patients with depressive illness or anxiety disorders. If your patient is showing symptoms of either, he/she may do well in one of these carefully monitored studies. FREE evaluation, lab testing and treatment if selected. Appropriate referral, if not. All results can be made available to referring physician. For further information or consult, call Walter Brown, M.D. or June Petrucci, RN, 274-4949, 272-1022.

MEDICAL SUITES FOR SALE OR LEASE

BARRINGTON: Maple Avenue Medical Center With Emergency Room, complete Medical Laboratory and Pharmacy Suites from 700 s.f. to 2900 s.f.

Available now for your custom layout

LINCOLN: Lincoln Medical & Health Center Located across from Lincoln Mall and connected with the Nautilus Health and Fitness Center

Suites from 1600 s.f. to 2000 s.f.

NEWPORT: The Borden-Carey Building

A revitalized historical brick structure abutting and connected to Newport Hospital Suites from 700 s.f. to 1500 s.f. Available now for your custom layout

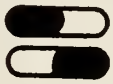
FOR INFORMATION CALL
RYAN, ELLIOTT & CO. OF RI, INC.
187 WESTMINSTER STREET
PROVIDENCE, RI 02903
401-331-0350

Thalidomide and D.E.S.

(They could happen again.)

Sometimes even the most promising drug may have unexpectedly adverse reactions in patients. Pre-market testing identifies most toxic drugs before release for patient-care use, but not all. Toxicity in some drugs can only be determined through adverse reactions detected among a larger number of patients over a longer period of time.

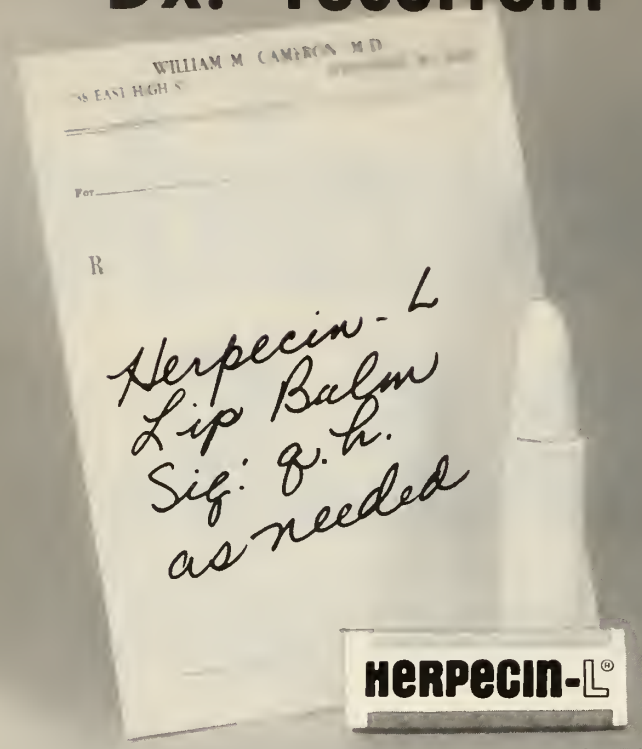
The plain truth is that a patient's health may be at risk. Adverse drug reactions cause death in approximately 30,000 patients annually in the United States alone. So, if you suspect an adverse drug reaction, please report it promptly. We may all live longer because you did.



The Adverse Drug Reaction Reporting Project
of the Rhode Island Department of Health

To report an ADR by phone, call **456-ADRS** weekdays between 9 and 5. To receive mailing forms and additional information, call the Health Department at 277-2901.

Dx: recurrent herpes labialis



"HERPECIN-L is my **treatment of choice** for perioral herpes." GP, NY

"HERPECIN-L appears to actually **prevent** the blisters . . . used **soon enough.**" DDS, MN

"HERPECIN-L®. . . a **conservative approach** with **low risk/high benefits.**" MD, FL

"Used at **prodromal symptoms** . . . blisters **never formed** . . . remarkable." DH, MA

"(In clinical trials) . . . **response** was **dramatic. HERPECIN-L** . . proven **far superior.**" DDS, PA

"All patients claimed **shorter duration** . . . at **prodromal symptoms** . . . HERPECIN-L **averted** the attacks." MD, AK

OTC. *See P.D.R.* for information. For samples to make your own clinical evaluation, write: CAMPBELL LABORATORIES, INC., P.O. BOX 812-MD, FDR STATION, NEW YORK, N.Y. 10150

In Rhode Island HERPECIN-L is available at all *Brooks, CVS, RiteAid* and other select pharmacies.

MEDICAL CLEARING BUREAU
1563 Fall River Avenue, Seekonk, Massachusetts 02110

A division of National Service Associates

Established for the Rhode Island Health Professions in 1932

COLLECTIONS — IN YOUR BEST INTEREST

8:30 A.M. to 4:30 P.M. WEEKDAYS

1-800-521-7974

Mailing Address: P.O. Box 402, Seekonk, Massachusetts 02771-0402

The Surgical History of Narragansett Bay

A Dialogue with History

John J. Byrne, MD

My first knowledge of medical practice in the Narragansett Bay area probably came while preparing a paper in 1958 on medicine at Plimouth Plantation at the request of Doctor Joseph Garland, our most revered past editor of the *New England Journal of Medicine*. It concerned the wife of Samuel Fuller, the first physician in Anglo America. About 30 years after his death from smallpox, it was requested in the town records of Rehoboth on June 3, 1663 that "voters agreed that Mrs. Bridget Fuller of Plimouth should be sent to see if she would be willing to come and dwell among us to attend the office of midwife, to answer the town's necessity which at present is great." She declined, however, and died the next year. This is the first time I realized that there was a Rehoboth, a part of which is now in Rhode Island.

John J. Byrne, MD is Professor of Surgery at Boston University School of Medicine, and Director of Surgery at Framingham Union Hospital, MA. He is currently working on a history of American Surgery.

Presented before the Providence Surgical Society on May 12, 1987. This is another of the series of historical papers published in the Journal *in celebration of the 175th Anniversary of the Rhode Island Medical Society.*

At about the same time I helped to found the Benjamin Waterhouse Medical Historical Society at Boston University and prepared the first talk of this Society on the life of this illustrious physician. He was born in Newport in 1754 and after a classical education apprenticed with Doctor John Halliburton in Newport prior to going to England to study with his cousin Doctor John Fothergill. As a young man in this thriving seaport he was friendly with the budding artist Gilbert Stuart. It is of interest that Stuart's father was brought to Newport by a Scottish physician, Thomas Moffatt, a student of Boerhaave in Leyden. Moffatt found practice difficult and tried growing tobacco and manufacturing snuff for which he needed the services of the millwright, Gilbert Stuart. I'm not going further into Waterhouse's later career in Boston.

This brief foray into early Newport and Rhode Island history led me to William Hunter, a relative of the famed William and John Hunter, who came to Newport in 1752 after an Edinburgh education. He delivered a series of anatomical lectures and practice until 1777. I also learned later at a Waterhouse meeting held in Newport, about Isaac Senter, who apprenticed with the above Thomas Moffatt and served as a Revolutionary War surgeon, being most famous for operating on Benefict Arnold's wounded leg outside Quebec. The role of Rhode Island physicians and surgeons during the Revoluation has been well reviewed by Charles E. Millard and Howard S. Browne.

From another Benjamin Waterhouse Society talk by Providence's eminent historian, Seebert J. Goldowsky, I learned about Rhode Island during the Civil War and particularly about the hospital at Portsmouth Grove and its many surgeons and physicians. He had previously reviewed the history of medical education in Rhode Island.

I discovered another Rhode Island connection last year when I gave a talk at St. John's Hospital in Lowell, Massachusetts and discussed the medical history of that once great city. One of its greatest stars for a while was Elisha Bartlett who had received an MD degree from Brown University Medical School in 1826, just 15 years after its founding, and went on to occupy departmental medical chairs at the Berkshire Medical Center, Dartmouth, Transylvania, Maryland, Vermont, Louisville, and finally Columbia.

It is of interest from the Rhode Island point of view that many of these schools were founded by a man from Rehoboth, Doctor Nathan Smith, who, after graduating from Harvard Medical School, went on to found medical schools at Bowdoin, Dartmouth, and Yale, and helped his son Nathan Smith found the school at Vermont. His son, incidentally, was also instrumental in the founding of Jefferson Medical College and the University of Maryland Medical School.

Bartlett was probably one of the most distinguished physicians of his time and was eulogized on many occasions by William Osler who claimed he didn't occupy just a chair of medicine, he occupied an "entire settee." His medical training was at Brown University, where anatomy and surgery were taught by the renowned Usher Parsons.

Born in Maine in 1788, Parsons apprenticed in medicine with Abiel Hall and Alex Ramsay. This was followed by an apprenticeship with John Warren, leading to his licensure by the Massachusetts Medical Society in 1812. His naval experience with Perry at Lake Erie made him a national figure. He returned to civilian practice in 1820 at Dartmouth and finally, in 1822, at Providence. Shortly thereafter, he married Oliver Wendell Holmes' older sister who, unfortunately, died in three years, leaving him with one son. His influence at Providence was profound. His career was briefly reviewed by Thomas Perry and is to be the subject of a full biography by Seebert J. Goldowsky.

Conversation

I was thinking of Parsons one evening, imagining his experiences at Lake Erie, and I think I must have dozed off. Suddenly a face appeared before me, and a man walked up to me. He had all the appearance of Usher Parsons. He looked at me with his clear eyes and said "Welcome to Providence. I'm glad you accepted the invitation to address our Surgical Society. Tell me, what is the latest news from Boston?"

"Well," I said, "it's probably no different from the rest of the country. Our surgeons don't seem to be as busy as they used to be. The HMOs* are taking over private practice; DRGs† are cutting into hospital finances; medical students are going into super specialities; medical education is horribly expensive; and malpractice is driving costs skyward."

"Whoa, now," Parsons said, "you're touching a lot of things I know nothing about. Tell me about some of them."

Operations

"I will, but first tell me about your surgical career."

"Well, you know," he said, "I published my list of operations in *Transactions of the Rhode Island Medical Society*."

"Yes, Dr Parsons, I read your statistics of the large surgical operations and was very much impressed. You trepanned four times in cases where there was 'abolition of the senses,' and you lost two patients and saved two. You wisely said that, if there were not 'abolition of the senses,' you should not trepan. Your one case of lithotomy was quite spectacular, and there was no mortality in spite of the fact is was performed in very hot weather during July of 1846. I was impressed with your operations on cancerous breasts — sixteen patients were operated upon and apparently four were cured. This figure would be very good today. You performed 24 amputations of the large limbs with only two deaths, a very commendable mortality. I noted also that you stated you used ether in only one case."

Parsons said, " I never could get used to that stuff. I heard of that operation by MacDowell in 1809 — what's become of it?"

"Well, a lot of surgeons began to remove ovarian cysts, particularly after the operation was made painless under ether anesthesia in 1842. It became safer. Doctor John Homans, a Boston surgeon, reported a low mortality and Doctors Burnham and Kimball of Lowell a 20 per cent mortality. As a matter of fact, the first two ovariotomies in Rhode Island were performed by

*Health Maintenance Organizations
†Diagnostic Related Groups

Doctor Burnham of Lowell upon patients of Doctor George Collins in 1862 and 1864.

There were many spin-offs from this operation. For instance, the first gallbladder operation was performed at Indianapolis by John S. Bobbs in 1867. He opened the right lower quadrant for a suspected cyst and found a dilated gallbladder. "As a matter of fact," I said, "MacDowell's ovariotomy opened the way for all the abdominal surgery we do today."

Parsons said, "Have all of these operations been successful and necessary?"

"Now you begin to sound like a modern quality assurance person!"

"What's quality assurance?"

I said, "I might go into that at a later date. Let's go on with the story about operations. Some of them didn't pan out too well and have been, happily, forgotten."

"Tell me more," said Usher, "I like a little gossip."

"Well, when ovariotomy became painless and safer and surgeons got used to palpating the ovaries, there came an urge to take them out even if they were normal. A distinguished southern surgeon from Rome, Georgia, and a graduate of Jefferson Medical School in 1857, Doctor Robert Battey, following a distinguished career as a Confederate surgeon, settled down in his home town where 14 babies (8 living) blessed his marriage. Whether this had some affect on his career I don't know, but in 1872 he spayed his first lady who had pelvic complaints and neuralgias."

Parsons said, "It's hard to believe that, I bet no Providence surgeon would do such a thing — imagine — unsexing a woman!"

"Battey felt that 'no part of the human body ought to be invested with such dignity and value that it may not properly be sacrificed for the welfare of the whole.' George W. Porter of Providence in 1880 wrote a paper on the operation. 'It made sense in the so-called hysteroneuroses. Patients with severe menstrual pain would become shattered neurotic patients and the premature menopause would relieve such symptoms.' It soon was done for epilepsy and some types of insanity such as melancholia."

"Eventually, this operation for psychiatric illness disappeared, but not for physiologic illness. It continued to be done for fibroids, since it was an easier operation than the formidable and dangerous hysterectomy."

Anita Tyng, a Providence surgeon, reported a very interesting case of a young lady with severe menstrual difficulties and a large fibroid uterus, who on January 8, 1880, was operated upon under a Codman and Shurtleff atomizer carbolic spray. Her assistants were Doctors Belcher, Weaver, Tomlinson, and Crawford (the latter was a resident physician in the New England Hospital for Women in Boston Highlands). These ladies had all carefully bathed with carbolized water and wore fresh clean calico dresses. The ligatures were also carbolized; the instruments were new and were laid in carbolized water before being used. It was a bright day, and the sun shone directly across the abdomen. A midline incision was made between the umbilicus and the pubis. Examination revealed a large fibroid uterus. The right ovary was found perfectly healthy, but the left one was not in its normal position and was not found. The incision was therefore enlarged, and it was found higher in the abdomen. She then removed both ovaries. Eventually the patient was discharged in healthy condition. The mass in the fibroid uterus receded in size. She felt this was a much safer operation than trying to do a hysterectomy. However, hysterectomy first performed by the Lowell surgeons Kimball and Burham in 1855, became safer, and ovariotomy for fibroids disappeared.

The attacks on the female organs continued. In cases of dysmenorrhea and sterility, if the cervical canal were tight or crooked, the cervix was divided. From the opposite point of view Emmet's operation came in vogue. When there were pelvic pains and excessive neurological symptoms and if the cervix were hypertrophied, ulcerated or engorged, the cervix should be incised and the raw edges approximated with wire, silk, or catgut sutures. This led Clifton Wing to report in the *Boston Medical and Surgical Journal* that these be branded as "unnecessary surgical operations." In respect to the uterus he said, "It seems that what is, is wrong, and what is not, ought to be brought about."

Eventually these operations ceased, but surgeons still had their eyes on the pelvis. Even until very recently, if a surgeon found that the uterus was retroverted or antroverted, all means were used to keep the uterus in an upright and manly position. We are all familiar with the Baldy-Webster procedures and the classic Alshausen procedure where the round ligaments were tightened either anteriorly or posteriorly to bring the uterus up into its so-called "normal state."

"Tell me more about the operations that you people are now doing. Are they still doing the operations I used to do — amputations and lithotomies?"

"It's interesting, Dr Parsons, what has happened to surgery. Many operations have come, but few have stayed. Many are happily forgotten. The operations based on anatomical causes have pretty much remained intact. Amputations are still being performed, but on a much lesser scale now that we've developed a way to improve circulation to legs by surgical procedures. Some of the amputations went a bit too far, as the translumbar amputations reported by Dr Henry "Tom" Randall, lately the Professor of Surgery at your old stamping ground. Trephining has continued. For instance, in your own home town, not too many years after your career was over, Dr Charles O'Leary was trephining for fractures associated with epilepsy. It has now expanded to craniotomy. Lithotomy continued for a great while, and Dr Gardner of our city in 1878 removed a 12 inch stone under ether anesthesia. It was complicated by sloughing of the rectum. Eventually the wound healed. However, Dr Bigelow in Boston invented a new machine which was going to eliminate such surgery. It soon spread to Providence where, in 1879, Dr Caswell, after demonstrating a lithotomy performed by the lateral operation, demonstrated Dr Bigelow's new lithotrite evacuating bulb. He felt that this was the operation of the future. Eventually, however, this went into disuse and surgeons went back to removing stones by direct approaches on the kidney, ureter, or bladder. But now there is a new invention whereby kidney stones are again being crushed using sound waves.

"So basically the operations for tumors, obstructions, trauma, and evacuation of abscesses and inflammatory processes continue. There are also operations on the heart and blood vessels. There are even some new anatomical procedures such as transplantation."

"Well, what do you mean by that? You mean like Damian and Cosmos?"

Parsons was, of course, alluding to the well known Saints Damian and Cosmos — surgeons who cut off the leg of a dead black man and sewed it on a white man. "Fortunately we have a better tissue typing; we can transplant numerous organs, beginning with the kidney, and spreading into the liver, lungs, and heart."

Parsons said, "I wish I were doing surgery again. It sounds fascinating."

I said, "Yes, but there are a lot of operations that didn't last, and the ones most apt to disappear were those based on physiology. All physiological processes are basically biochemical in nature, and eventually drugs are discovered and some brilliant operations cease to exist. One of the classic examples is thyroidectomy, not only for goitre or bronchocele as you would call it, but also for thyrotoxicosis. This period of surgery has been called by some the golden period of surgery as surgeons learned to remove the thyroid, beginning with Kocher, and pioneered by our own American surgeons such as Crile, the Mayo Brothers, Lahey, and others. Such surgery became safe and was the beginning of many of the medical institutions, such as the Mayo Clinic, the Crile Clinic, and the Lahey Clinic. However, medical scientists found ways of altering thyroid function, and now these operations are rarely done except for tumors or for very large masses.

"Another class of functional operation was for ulcer disease. Moynihan and others were quick to take up the German operation of gastroenterostomy for ulcers, and in the next 40 or 50 years a whole series of operations was attempted to try to cut down the acidity of the stomach so that peptic ulcers would not form. The gastrojejunostomy failed because of recurrent ulcers, gastrojejunocolic fistulas, and gastro-ileostomy. Eventually, we all listened to Wangensteen's scientific approach. He produced the disease in animals using beeswax and histamine and finally found that only a high subtotal gastrectomy would salvage such ulcers and prevent recurrences. However, there were many problems associated with subtotal gastrectomy, and over the years many procedures were designed, including sleeve resection of the stomach, proximal gastrectomies, and the ingenious Aylot procedure whereby the alkaline juices in the jejunum were poured into the top of the stomach and the stomach would empty out into the other side of the jejunum."

"And let us not forget the gastric freezing machines!"

"These procedures, of course, all had their problems. Peptic ulcer surgery has now become very simple and practically disappeared because of drugs produced by modern pharmacology.

"A third example is the operation designed by Dr. Smithwick for hypertension where he took out the greater or lesser splanchnic nerves to improve this serious disease. However new drugs were discovered which took the place of the operation, and it, too, is on the list of forgotten operations.

"Attempts to cure disease by cutting nerves continued, and vagotomy was used even to try to cure Crohn's disease, and ulcerative colitis by frontal lobotomy. The collapse therapy of tuberculosis could be abetted by phrenicectomy,

although J. Murray Beardsley would wisely caution against its use in 1934.

"The operations based on sound physiology disappeared slowly with the advent of newer drugs. However, operations based on false physiology disappeared with newer knowledge, such as we mentioned, with the ovariotomy procedure. For instance, there was a condition once known as hour-glass stomach for which a satisfactory operation was developed. Another abdominal complaint was prolapse and ptosis of the stomach. There were two varieties: one a disease of the young where there was strong abdominal musculature, and another in the old multiparous patients who have very lax abdominal walls. Several types of operations were designed for this problem. Fortunately, the problem seems to have vanished with the disappearance of corsets and the wasp waist.

"The concept of chronic intestinal stasis, or so-called auto-intoxication proposed and advocated by Arbuthnot Lane of Guy's Hospital in London, had a longer reign. In order to cure this condition, which was supposed to cause numerous conditions, such as pernicious anemia, nephritis and diabetes, and sometimes just not feeling well, he suggested that the whole right colon be bypassed by an ileosigmoidostomy, and in some cases he even did a resection of the colon. The concept was taken by many American surgeons, and A. J. Oschsner had a unique operation for bypassing the entire colonic contents. One would also have to look for other foci of infection, and remove the teeth, tonsils, gallbladder, and appendix. These operations were performed in all the clinics in the United States. The spleen was often implicated, and for some reason or other splenectomy was the operation for pernicious anemia, at which time of course, the appendix would also be removed. Eventually the colonic bypass resections disappeared, but the routine removal of gallbladder, teeth, and tonsils as foci of infection was slower to disappear. For many years, even in recent times, every hospital had a "Gallbladder Bill" who would take out the gallbladder at the drop of a hat for patients who weren't feeling well with various complaints.

"Other more modern operations based upon false physiology include internal mammary artery ligation for coronary disease, carotid body excision for asthma, and resection of the aortic bifurcation for Leriche's syndrome.

"The operations for psychiatric reasons have all disappeared. But there were lingering attempts in our own generation to cure such diseases by surgery, most noteworthy being Freeman's pre-frontal lobotomy in the 1950s."

Infections

"Well, that's an interesting story you tell, Dr Byrne, about happily forgotten operations. I did note that the mortality was quite low. What made these operations so safe?"

"The big thing, of course, is the germ theory of disease."

"What are germs?"

"Germs are small organisms that live in the air and all over the earth and creep into wounds and cause pus."

"You mean 'laudable pus' is caused by germs?"

I said, "That's right, and there really should be no 'laudable pus.' All wounds should heal by first intention. The man most responsible for learning about this was Joseph Lister."

"I can't believe that our Providence surgeons would believe in a theory like that."

I said, "Well, they did, eventually. One of the first to take up the work was Dr Caswell when, in 1878, he presented and published a paper on Lister's method. However, the germ theory wasn't accepted until the beginning of the 20th century. Dr Frank Fuller of Providence read a paper in 1884 on the cause of puerperal fever and its prevention. Dr Newell considered the septic nature of the disease unproven and opposed all details of treatment growing out of germs believed in but not seen. Dr Ariel Ballou objected to too much meddling with nature's processes. You remember him?"

"Yes, I remember Ariel. He spent a year training with me before he went with Dr Childs at the Berkshire Medical Center. He then came back to Woonsocket to practice and was mixed up with Dorr's Rebellion."

"Well," Parsons said, "we did have a lot of infection. I think the worst was diphtheria. It was horrible seeing those people suffocating. If only we could have restored their breathing tube."

"Oh," I said, "there was a man by the name of Dr O'Dwyer of New York who invented a way of putting tubes in the pharynx, and this system was taken up all over the United States and saved many lives. In Providence Doctors Mitchell, Terry, Peckham, and Fuller were all intubating. However, the final demise of the disease was due to the antitoxin which was developed against the disease."

"Eventually in Rhode Island the germ theory was no longer a theory. As Dr Horace G. Miller stated in an address before the Rhode Island

Medical Society, 'A theory is only a scaffolding on which to stand while building the structure of a science. When a building is built, the scaffolding is torn away. The germ theory is a theory no longer necessary. Let us cast it aside and behold the science of Pathological Bacteriology, the knowledge and study of disease-producing germs. The building is firmly founded and is complete as to its external form at least. The details are just being brought out and developed.' "

Families

"While trying to prepare some idea for this talk I got some good information from a Presidential Address given by your son Charles Parsons. Incidentally, there have been a lot of doctor/son, and even grandson, relationships in this town, haven't there?"

He said, "It all began with the Bowens and Dan Jones and his progeny. I hope it continues."

"Yes," I said, "there are many medical families on the contemporary scene: Porters, Healeys, Hindles, Ashworths, Corveses, Gibsons, Wesselhoefts."

Today's Surgeons

"I was surprised at the few operations you did over the course of your lifetime. That's not really a lot of operations for the busy surgeon you were supposed to be. Ira Rutkoff, one of our ex-Boston University residents now practicing in New Jersey, has just furnished a study of how busy surgeons are today. I bet you can't guess the most frequently performed operation."

Parsons said, "Probably an amputation or a lithotomy."

"No, it's a Cesarian section."

"Don't doctors know how to deliver babies any more? All you need for a safe delivery is a lancet and a catheter."

"Times have changed, Usher, now it's complicated by malpractice, patient's expectations, and a host of other problems. The second most common operation is hysterectomy. I won't run down a complete list, but a few are as follows: 3, D & C, 4, cataracts; 5, hernias; 6, surgery of the Fallopian tubes for sterility; 7, cholecystectomy; 8, tonsillectomy; 9, salpingectomy; and 10, prostatectomy."

"My, what a lot of operations the surgeons are doing. They must be busy."

"Not as busy as it seems. The average surgeon now performs 161 operations a year; but the general surgeon, divorced from everything except gastrointestinal surgery, performs only 139 operations a year."

"What is going to happen to the general surgeon?"

"The solution lies in three areas: limiting training opportunities for new general surgeons; reclaiming the operations from gynecology, orthopedics, plastic, hand, head and neck, trauma to the extremities; expanding the duties of the general surgeon in intensive care, surgical nutrition, oncology, trauma, and care of emergencies; and maybe the elimination of residency programs in many hospitals with the assisting and other chores being done by practicing surgeons, as it used to be. I remember reading about cases at Providence where four or five surgeons would work together on a single case. At one of the operations on the 14th of March in 1893, Dr Keefe operated with his assistants, Collins, Noyes, Mitchell, Chesborough, and O'Neill. The first interval appendectomy in Rhode Island was also performed by Keefe, and his assistants were Collins, Dunne, Mitchell, Noyes, Blake, Mahoney, Barry, and O'Neill. This system has now disappeared, and many of the hospitals have residents."

"What are residents?" asked Parsons.

"Well, residents are a new way of training surgeons. In your day you were apprenticed to someone, then you assisted someone, then you got to do your own operations. Today the young surgeons apprentice with a lot of surgeons and learn to do the operations much more quickly, and as soon as they start practice they expect to be busy."

Board of Registration

"I am curious, though, why you were so late developing a Board of Registration in Medicine."

"Well," said Parsons, "we never really felt it necessary."

I said, "That seems to be true. In 1888 Dr Eldredge said, 'The petition before the Legislature two years ago for regulating the practice of medicine requiring evidence of qualification and a form of registration before assuming the duties and privileges of a physician did not originate in a vote of this Society. Many of its members advocated in favor of passage of the act, but it was misunderstood by the public to be looked on as a plan to secure a monopoly rather than as a measure to protect the people from the imposition of all sorts of quackery. Some of our oldest members were opposed to any legislation of the kind saying it was not Rhode Island's way. It was inalienable right of the people to be humbugged

if they so chose. In the meantime, the matter rests without interference on our part when the people shall ask for something of this kind for their own protection we shall be glad to see it.' As one member said when told 'all the other states are doing this,' . . . 'we were the last state to ratify the constitution so there is no reason why we shouldn't be the last state to do this.' "

"You may have been right. In our state the Board of Registration has become very powerful. We all have to report our problems, errors, and accidents to them. In some cases they are even dictating how certain specialties shall be practiced."

"Why," said Usher, "that's horrible. What does the State Legislature know about the practice of medicine? I suppose all the Board of Registration members are doctors."

I said, "Of course not."

"How then can they define proper practice? Medicine is changing constantly. How can there be a cookbook of medical knowledge on how to act? It reminds me of the time when the works of Galen were followed leading to an appalling dogmatism and infallibility almost religious in character."

"We can sympathize with Paracelsus as he burned Avicenna's *Canon* at Basel in 1527 and can admire the tenacity and brilliance of Vesalius in overthrowing the Galenic traditions. The further Renaissance and scientific revolution has brought medicine, and surgery in particular, to its modern pre-eminence. Legislative impositions and restrictions will impede progress by deterring the creative and innovative impulses."

"Today it is not religous dogma or lack of scientific tradition that is reviving the infallibility or codification of current standards here. Instead, it is fear of the legal profession in its drive for quick riches, and the soaring costs of malpractice. These are driving outside agencies to develop standards of care. But whose standards? Quite often the standards set down occur in text or article. Which text for surgery — Schwartz's, Sabiston's? As I was thinking about this I looked across the wall and saw one of my favorite paintings, *The Samuel D. Gross Clinic* by Eakins. He was the accepted leader of his day and wrote the classical textbook of his time. How would we be forced to practice if his great text became the standard against which we would be challenged if we practiced 100 years ago."

Famous Quotes

Parsons said, "I have heard of Samuel Gross. Some of my students went to Jefferson to finish their medical education. He certainly is a magnificent surgeon."

"Yes," I said, "but he was not omnipotent. Let me tell you a few of his infallible remarks:

" 'For the reducible hernia, the best remedy is a suitable truss.'

"In discussing cancer of the stomach: 'In view, therefore, of the facts that incipient cancer is difficult to diagnose, an extension in adhesions, glandular contamination, and secondary growths are frequent complications, and three-quarters of the patients have heretofore perished from the effects of the operation. . . . And finally, the procedure has materially shortened instead of prolonging life, and I am of the opinion that gastrectomy for cancer will soon fall into desuetude and that its details need not, therefore, be described.'

"Of the pancreas: 'Lesions of the pancreas possess little of surgical interest. The deep situation of the organ places it beyond the reach of the ordinary causes of disease and accident and renders it extremely difficult to discriminate between its own malady and those which affect the neighboring viscera.'

"As regards liver injuries: 'In the treatment of the wounds of this organ the great object is to limit inflammation by the most quiet, gentle enemas and careful restriction of the diet. If the patient be young and robust, the use of the lancet may be required; otherwise it will be better to be contented with leeches, fomentations, and blisters.'

"With regard to Battey's operation: 'The results of this operation are generally gratifying.'

Medical School

I said, "Dr Parsons, you have been a noted teacher in this city; you were first on the faculty of Brown University before it ceased. Could you tell me why Brown University dissolved its Medical School?"

"Well," he said, "it had something to do with payment of the faculty members. Most of the faculty were clinical physicians and the President of Brown University at that time wanted everyone to be an employee of the University. This could not come about and the Medical School was disbanded. I think it was a shame."

Well, it certainly has a modern ring.

The Town-Gown Syndrome exists today in most areas to some degree whenever a medical school recruits a faculty to practice medicine or surgery. It has recently been analyzed quite lu-

cidly by Robert G. Petersdorf, a leader in the Association of American Medical Colleges.

Non-Surgical Time

"Tell me though, how did you spend the rest of your time when you weren't operating? I noticed while reading a history of the medical profession in Rhode Island written by you, Issac Ray, and George Collins in 1859 that many Providence physicians had secondary sources of income: "Pardon Bowen embarked as the surgeon of a privateer and on one occasion secured enough prize money to 'make amends' for this career."

"Amos Throop, at the beginning of the revolution married Mary Crawford, an expert on drugs and medicine. She convinced him to order an extraordinarily large shipment from London — as much as he could afford. To be sure of this order, he sent it on two vessels. In time he received not one shipment, but two! Needless to say this error earned him a generous income. He also became President of the Exchange Bank.

"William C. Bowen (nephew of Pardon Bowen) studied with Sir Astley Cooper and became Professor of Chemistry at Brown. He experimented on a bleaching "liquor" and laid the foundation for the famous bleaching establishment of Rhode Island. Unfortunately, the inhalation of these noxious vapors destroyed his lungs and he died at the age of 30 in 1815."

Parsons continued, "I taught over fifty private medical students. I kept up on the practice of dissection. I was active in affairs of the American Medical Association being a delegate to it and chairman of many of its committees. In 1854 I was the first Vice-President. On top of this I worked hard for the Rhode Island Medical Society and was its President from 1837 through 1840. I wrote numerous articles and journals and received four Boylston prizes and one Fiske award. I was active in the organization of the Rhode Island Hospital. Besides medicine, of course, I had many other interests having to do with natural science. In geneology I published the memoirs of my ancestors including the life of Sir William Pepperell, published in 1855 and republished in London. I continued my anthropological studies being very interested in the remains, customs, and language of the Indians in this part of the country.

"In addition, I kept up my historical interest in the Battle of Lake Erie and gave many discourses concerning it in many parts of this country. I related some of my experiences to Frank H. Hamilton, the great surgeon in Brooklyn, New York in response to a letter from him. At the battle of Lake Erie on 10th of September 61 men on board the Lawrence were wounded. There were 11 cases of compound fracture besides simple fractures, gunshot wounds, and extensive lacerations. Among them all, several amputations were required.

"To the wounded on the Lawrence were added, after two days, 23 from the Niagara and a dozen from the small vessels. The whole number of patients requiring a recumbent position on the deck was about fifty. The only shelter over the wounded was an awning that served as a screen from the sun and canvas to spread over them when it rained. They remained on the ship 14 days after the action, and then landed at Erie and lodged in a large unfinished court house and remained there until cured. Of the 96 wounded only three died and these were cases so severe in nature that a surgical operation was not deemed justified and they were left to linger out in misery for a few more days. This entire success I have ever felt warranted in describing to the purity of the air more than to any other cause. A second success worth of special notice was the delay of severe surgical operations until the system was entirely recovered from the shock of the injury.

"A third cause of success in this action was the plentiful supply of fresh provisions and fresh vegetables brought to the fleet from the shores of Ohio and a generous supply of wine and other cordials. Fourthly, there could be no doubt that cheerful and buoyant spirits occasioned by victory contributed not a little to recovery.

"I've just been reading about the battle." I said, "how lucky you were — one midshipman you were treating was torn out of your hands by a cannon shot. Five cannon balls pierced through your surgeon's cabin. When Perry left the disabled and ruined Lawrence to seek the unharmed Niagara you were left in the hold with the care of 61 wounded and surrounded by 26 dead men."

Parsons replied, "Jesse Elliott, Captain of the Niagara, was a coward and should have been shot. I thought we'd all be dead. Come down to the hold and see Captain John Brooks with me. His right hip has been carried away by cannonball. He's begging for a pistol to kill himself. Smell the smoke and gunpower, but don't slip on the blood."

At that moment I felt a burning agonizing pain in my right arm. I looked and saw blood and a large piece of radius protruding from below my elbow. "You've been hit," said Parsons, "we'll have

to amputate right now." His mates grabbed my arm and put me on the table. They bared my right arm to my shoulder, and Parsons got out his amputation knife, his catlin and saw, and started to make the classical circular incision through skin, muscles and tendons. I let out a blood curdling yell.

With that I felt a vigorous shaking motion. I heard a voice, my wife. "Johnny, what's wrong, you're having a nightmare. What happened?"

I said, "Parsons was going to amputate my arm."

"Who's Parsons?"

I said, "He's a great Providence surgeon." I was having a conversation with him. She said, "You'd better have a conversation with someone else." I did think about it for a long time afterward. There are a lot of Narragansett Bay men with whom I would have liked to have a conversation. There are many who need fuller biographies. Or perhaps in my ignorance many have had fuller treatment. I know we'll all be grateful to Goldowsky for what I am sure will be a magnificant biography of Parsons.

One man I would like to know more about was R. F. Noyes. In reading the *Transactions of the Rhode Island Medical Society* he wrote numerous excellent papers on a whole range of topics: pancreatitis, intestinal obstruction, and blood pressure. His best paper, however, was on perityphlitis. He described the right lower quadrant pain, vomiting, testical retraction, and absence of tenderness in typhlitis. This might progress to perityphlitis with tenderness and tumor. The thigh might be flexed. It would increase the temperature, produce chills, and accelerate the pulse. He assumed this was caused by appendiceal perforation. This would go on to abscess formation and might burrow along the psoas, along the inguinal canal, out the sciatic notch, or around the colon to beneath the diaphragm. His treatment was based on the German use of opium to quiet and splint the intestines, and when suppuration was felt to be present, incision and drainage. He quoted Willard Parker's five-day dictum and reported his successful case in 1882 that he had operated on with Dr Daniel O. King. He quoted two other Providence surgeons, C. T. Gardner and R. H. Carver, who also had experience with the Parker operation. At this time I can find no reference that Boston surgeons had been in print concerning it.

Soon Fitz would rename the process appendicitis and suggested operation as soon as perforation was diagnosed. He felt that to operate before perforation would yield little results, since it would be difficult to diagnose. The subsequent safety of appendectomy would be proven by McBurney, Richardson, Murphy, Fowler, and Ochsner. Many still did not like the new name of appendicitis, as it was a compound of Greek and Latin roots. Dr Munro, a Boston City Hospital graduate, was calling it "epityphlitis" in 1900. The first cases in Rhode Island of appendicitis as such with operation for removal of the appendix from an appendiceal abscess cavity was by George L. Collins. He was assisted by Dr J. W. Keefe. It was not too long before Keefe could report a whole series of operations for appendicitis both at the Rhode Island Hospital and at St Joseph Hospital.

Horatio R. Storer is another fascinating person, whose operation I will describe. He was the son of D. Humphreys Storer, pioneer obstetrician and gynecologist in New England and Professor at Harvard Medical School. Horatio graduated from Harvard Medical School in 1853 and Harvard Law School in 1868. He studied in Europe and was in private practice with Sir James Simpson for one year. After being assistant to his father, he briefly became head of the department of obstetrics at Berkshire Medical College until it closed in 1869. He then came back to Boston and became one of the first to teach gynecology as separate from obstetrics. He was physician to Boston Lying In Hospital, Carney General Hospital, and the New England Hospital for Women and Children.

With Dr Attlee of Philadelphia, Peasely of New York, and Kimball of Lowell he practically monopolized the ovariotomies in the United States and Canada. In 1872 following an attack of septicemia from which he barely escaped, he retired from Boston and spent several years in Europe and then retired to Newport. It is while there that the following operation was performed by him. He described an operation recently performed for a large fibroid cervical tumor completely filling up the vagina. The patient was anesthetized and placed upon her back on the table, and an ecraseur applied. The chain was held in position with the tips of the fingers of one hand introduced flatwise beside the tumor, while the screw was worked with the other, until a sufficient sulcus had been cut around the broad base to retain the chain from slipping. Shortly, however, so great was the resistance, the chain broke, and as it would have been impossible to reach the base of the tumor with any degree of exactness by either bent scissors or knife, further proceedings were for the time suspended. Four days

later, the same gentlemen being present, with the addition of Mr Malcolm Storer, a student of medicine, the operation was again essayed by Dr Storer, and successfully completed. When the chain of the ecraseur had cut itself away and the tumor could be rotated in the vagina like an orange, it was found that it could not be extracted in the usual manner. The straight forceps for traction was not available, but a strong straight hooked forceps in the grasp of the strong man utterly failed to deliver the tumor. Dr Storer then improvised a vectis by bending a large and stout iron spoon, but even this was ineffectual, though it neutralized the delaying effect of the vacuum behind by permitting air to enter above the tumor. He determined to do as he had done once or twice before in similar cases and produce expulsion by pressure superiorly and from within, in imitation of the powers of nature during the process of labor. Forcibly dilating the sphincter ani, he introduced his arm up to the elbow into the rectum, the fingers having to enter the sigmoid flexure before he could exert sufficient expulsive leverage anteriorly. Under this added force, with the vectis and forceps combined, he was able to deliver the tumor precisely as though it were a fetal head. The vagina was then plugged. The patient progressed without a single unfavorable symptom.

In answer to an inquiry whether such apparent disrespect to the rectum were surgically justifiable, Dr Storer replied that surgical justifiability was always to be decided by its results. The question was not so much was it advised by the textbooks and pursued by other operators, as what the occasion indicated, what the necessity required, and what the event proved; and, if necessary, "completing surgical operations within the vagina one could boldly insert the arm (in the rectum) nearly to the elbow."

There are other men I would like to know more about:

I would like to know more about G. E. Mason who performed the first operation at the Rhode Island Hospital (a resection of the maxilla). Parsons and all of the Narragansett Bay surgeons were present.

I would like to know more about Dr Dan King who was in the first class at Yale and was taught anatomy and surgery by Nathan Smith. Seven of King's sons and grandsons were doctors of medicine.

George P. Baker, a student of Usher Parsons, whose medical training was suspended at Harvard during the Parkman murder trial. From him we could find out more of the feeling of the students about the scandal.

From Dr Chase Wiggins we could try to find out more about his teachers, the Crosby brothers (Dixie and Josiah), of the famous New Hampshire family of physicians. This family was so well known in this state that many surgeons changed their name to Crosby, hoping they would benefit by the name change.

J. W. C. Ely was present at the first ether operation. I have since studied Hinckley's painting and accounts of the painting, and nowhere can I find where he was in the picture. He could have told me which of these people he was. Ely practiced over sixty years in Providence.

I would have enjoyed Walter Lee Munro (Brown AB 1879, MA 1882, Harvard Medical School 1885) and a graduate of the Boston City Hospital and Lying In Hospitals. His surgical mentors were a distinguished group — George Gay, David Cheever, William Thorndyke, Charles Homans. He was a personal friend of William Keen, William Halsted, Howard Kelly, Sir William Osler, O. W. Holmes, and the Mayos. He was a part of the scientific research team that developed the telephone.

George L. Collins was an outstanding physician. He pioneered in pathology and prepared exhibits of gross as well as microscopic specimens. He helped prepare the first tables of death for Providence from 1840-1854.

George W. Porter began the practice of gynecology in a little hut in back of the Rhode Island Hospital. This was at a time when only the poor went to the hospital. Operations on the middle class were done at home by Providence surgeons; the wealthy could summon surgeons from a distance — Maurice Richardson from Boston, John Erdmann from New York, Deaver from Philadelphia, and John M. Finney from Baltimore.

Porter's problems in developing gynecology were similar to those elsewhere. At the Boston City Hospital Drs Boardman and Chadwick were assigned a small room in the Lodge or gate-house in 1873. In 1890 the new outpatient department was built and more room was available, and finally in 1890 a nurse was provided to prepare the patients for examination and treatment. In 1898 they were finally given a service in the hospital.

Charles O'Leary, an emigrant from Ireland, became Professor of Latin and Greek in Maryland, and then in chemistry in Cincinnati, Ohio, where he studied medicine at the Medical College of Ohio, and finally at the Long Island Col-

lege Hospital in Brooklyn. He began the practice of surgery in Cincinnati. At the outset of the Civil War, he went to Washington, where he served in most of the Eastern campaigns and in the peninsular in Maryland and finally became medical director of the entire left division of the Army commanded by Burnside.

Another surgeon, John W. Keefe, was one of the founders of the New England Surgical Society. Born in Worcester on April 25, 1863, he began his medical training at the University of Michigan 1882-1883, and finished at the medical college of New York University in 1884. After interning at Bellevue, he went to Providence and established himself in practice at the Rhode Island Hospital, where he served as surgical extern in 1886 to 1897. He went up the ranks to visiting surgeon in 1897, which position he held for 22 years, until he was appointed consulting surgeon in 1919. He was also active in the County of St John's Children's Hospital where he served until resignation in 1905. He built his own John W. Keefe surgery in Providence in 1913 and did most of his private surgical work at his own hospital. He was one of the founders not only of the New England Surgical Society, but also of the American College of Surgeons. He is considered to be the first practitioner in Rhode Island to give up the general practice of medicine and devote himself solely to the practice of surgery. He pioneered in abdominal surgery, and his operation for pyloric stenosis preceded the Ramsted operation. He was obviously in demand through the state, since he was consulting surgeon to the Rhode Island Hospital, St Joseph's, Charles V. Chapin, Providence Lying-in, South County, Westerly, Woonsocket, and Pawtucket Memorial Hospitals.

I would like to know more about the other founding members of the New England Surgical Society — Edgar B. Smith and Arthur T. Jones. Keefe would become President of this Society in 1925, to be followed by Lucius G. Kingman in 1936, and Emery M. Porter in 1949. As recorder of the New England Surgical Society it has been my privilege to know many of the recently deceased members of this State — Doctors Hermon C. Pitts, Hartford Gondoware, Jesse M. Gibson, J. Murray Beardsley, Wilfred Pickles, Clarence E. Byrd, William P. Davis, John B. Ferguson, William A. Mahoney, Edward S. Cameron, Robert R. Baldridege, James C. Callahan, Orland F. Smith, Charles W. Cashman, Jr., Lester L. Vargas, and George W. Waterman.

As I read the *Transactions of the Rhode Island Medical Society,* the *Providence Medical Journal,* and the *Rhode Island Medical Journal* while preparing this manuscript, I was impressed by the historical perspective of the earlier physicians. As I progressed into the modern era, the biographies became sketchier and even non-existent. Perhaps the earlier surgeons had more time on their hands. But it is difficult to find material to flesh out the more recent personalities, such as Lucius Kingman, Emery Porter, Frank McEvoy, Joseph O'Connell, Gondoware, Beardsley, Pickles, Baldridge, Callahan, and George Waterman. Peter Pineo Chase secured better treatment, probably because he was editor of the *Rhode Island Medical Journal.* Current events, such as the development of the Brown University Medical School's Surgical Department or a history of the Providence Surgical Society, deserve to be chronicled.

I hope there are surgeons who will develop the rich lore of Narragansett Bay surgery. I believe that if we treasure our past, and preserve the present, the future will be secure. History is a guide for the future. The good deeds of our predecessors serve to stiffen our backbones as we meet today's challenges and to serve as a scaffolding for the next generation of surgeons.

NOW UNDER DEVELOPMENT
at
ASHLEY DOWNS
BIOPHARMACEUTICAL LABS

An entire new line of **NONANIMAL SOURCE** Insulins
Pūrinsulin Human® ..... nonanimal rDNA source
Pūrinsulin Pork® ..... nonanimal rDNA source
Pūrinsulin Beef® ..... nonanimal rDNA source
Pūrinsulin Beef/Pork® ..... nonanimal rDNA source

Human Tissue Plasminogen Activator (tPA)
Plasminase® ..... chemically synthesized gene product

Human Erythroprotein (EPO)
Erythrōten® ..... chemically synthesized gene product

In R&D: Factor VIII; Interleukin-2; Growth Hormone

Ashley Downs Biopharmaceutical Laboratories
A NEW BIOTECH FACILITY
IN RHODE ISLAND

correspondences to:
Ashley Downs Biopharmaceutical Laboratories
909 North Main Street
Providence, RI 02904

STARKWEATHER & SHEPLEY

PROVIDES MORE MALPRACTICE INSURANCE FOR RHODE ISLAND DOCTORS THAN ANY OTHER AGENCY....ANYWHERE

PLUS insurance for....
partnership
disability income
worker's compensation
fire/theft/auto
and group insurance, pensions, benefits

Since 1879

STARKWEATHER & SHEPLEY, INC.
155 South Main Street
Providence, Rhode Island 02903
(401) 421-6900

LAW OFFICE OF HERBERT M. ADAMS, J.D.

GENERAL LAW PRACTICE
MEDICAL COLLECTIONS

GOVERNOR FINANCIAL CENTER
P.O. Box 2502
285 Governor Street
Providence, Rhode Island 02906
(401) 421-1364

Do You Know an Impaired Physician?

Treatment of physicians for alcohol addiction shows a favorable outcome in 83 per cent of cases, and treatment of physicians for drug addiction has a 95 per cent success rate. More than 70 per cent of the physicians entering treatment return to the active practice of medicine.

The Rhode Island Medical Society Committee on Impaired Physicians, chaired by Dr Herbert Rakatansky, meets monthly. It is a standing committee of the Society charged with "helping physicians whose professional judgments and capabilities are impaired by their difficulties with chemical dependency or other illnesses."

The Committee handles inquiries in *complete confidence*. If you know of a physician who needs an advocate and support in obtaining necessary treatment, please call or write Dr Rakatansky c/o The Committee on Impaired Physicians, Rhode Island Medical Society, 106 Francis Street, Providence 02903 (401/331-3207).

In acute and chronic edema due to CHF

FOR PREDICTABLE CONTROL

- **Less potassium loss for a given amount of sodium excretion than with furosemide[1-3]**
- **Predictable dose response[4]**
- **Diuresis completed hours faster than with furosemide after oral dosing[5]**
- **Better GI absorption[6,7]**
- **Early evening dosing helps prevent nocturnal dyspnea**

Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets, 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

As with all loop diuretics, excessive doses of BUMEX can lead to profound diuresis with water and electrolyte depletion, including hypokalemia, so serum electrolytes should be monitored.

References: 1. Flomenboum W: *Am J Cardiol 57*(2):38A-43A, 1986. 2. Brater DC, Fox WR, Chennovasin P: *J Clin Pharmacol 21*: 599-603, 1981. 3. Iber FL, Baum RA: *J Clin Pharmacol 21*: 697-700, 1981. 4. Henning R, Lundvoll O: *Eur J Clin Pharmacol 6*: 224-227, 1973. 5. Physicians' Desk Reference, 40th ed. Orodell, NJ, Medical Economics Company, 1986, pp. 939, 1480. 6. Pentikoinen PJ, *et al*: *Br J Clin Pharmacol 4*: 39-44, 1977. 7. *Lasix, A Review*. Somerville, NJ, Hoechst-Roussel Pharmaceuticals, Inc., 1980.

BUMEX®
(bumetanide/Roche)
0.5-mg, 1-mg and 2-mg scored tablets
2-ml ampuls, 2-ml, 4-ml and
10-ml vials (0.25 mg/ml)
Before prescribing, please consult complete product information, a summary of which follows:

WARNING: Bumex (bumetanide/Roche) is a potent diuretic which, if given in excessive amounts, can lead to a profound diuresis with water and electrolyte depletion. Therefore, careful medical supervision is required, and dose and dosage schedule have to be adjusted to the individual patient's needs. (See under DOSAGE AND ADMINISTRATION in complete product information.)

INDICATIONS AND USAGE: Edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome.
Almost equal diuretic response occurs after oral and parenteral administration of Bumex. If impaired gastrointestinal absorption is suspected or oral administration is not practical, Bumex should be given by the intramuscular or intravenous route.
Successful treatment with Bumex following instances of allergic reactions to furosemide suggests a lack of cross-sensitivity.
CONTRAINDICATIONS. Anuria. Hypersensitivity and in patients in hepatic coma or in states of severe electrolyte depletion. Although Bumex can be used to induce diuresis in renal insufficiency, any marked increase in blood urea nitrogen or creatinine, or the development of oliguria during therapy of patients with progressive renal disease, is an indication for discontinuation of treatment.
WARNINGS: Dose should be adjusted to patient's needs. Excessive doses or too frequent administration can lead to profound water loss, electrolyte depletion, dehydration, reduction in blood volume and circulatory collapse with the possibility of vascular thrombosis and embolism, particularly in elderly patients.
Prevention of hypokalemia requires particular attention in patients receiving digitalis and diuretics for congestive heart failure, hepatic cirrhosis and ascites, states of aldosterone excess with normal renal function, potassium-losing nephropathy, certain diarrheal states, or other states where hypokalemia is thought to represent particular added risk to the patients.
In patients with hepatic cirrhosis and ascites, sudden alterations of electrolyte balance may precipitate hepatic encephalopathy and coma. Treatment in such patients is best initiated in the hospital with small doses and careful monitoring of the patient's clinical status and electrolyte balance. Supplemental potassium and/or spironolactone may prevent hypokalemia and metabolic alkalosis in these patients.
In cats, dogs and guinea pigs, Bumex has been shown to produce ototoxicity. Since Bumex is about 40 to 60 times as potent as furosemide, it is anticipated that blood levels necessary to produce ototoxicity will rarely be achieved. The potential for ototoxicity increases with intravenous therapy, especially at high doses.
Patients allergic to sulfonamides may show hypersensitivity to Bumex.
PRECAUTIONS: Measure serum potassium periodically and add potassium supplements or potassium-sparing diuretics, if necessary. Periodic determinations of other electrolytes are advised in patients treated with high doses or for prolonged periods, particularly in those on low salt diets.
Hyperuricemia may occur. Reversible elevations of the BUN and creatinine may occur, especially with dehydration and in patients with renal insufficiency. Bumex may increase urinary calcium excretion.
Possibility of effect on glucose metabolism exists. Periodic determinations of blood sugar should be done, particularly in patients with diabetes or suspected latent diabetes.
Patients should be observed regularly for possible occurrence of blood dyscrasias, liver damage or idiosyncratic reactions.
Especially in presence of impaired renal function, use of parenterally administered Bumex should be avoided in patients to whom aminoglycoside antibiotics are also being given, except in life-threatening conditions.
Drugs with nephrotoxic potential and bumetanide should not be administered simultaneously.
Since lithium reduces renal clearance and adds a high risk of lithium toxicity, it should not be given with diuretics.
Probenecid should not be administered concurrently with Bumex.
Concurrent therapy with indomethacin not recommended.
Bumex may potentiate the effects of antihypertensive drugs, necessitating reduction in dosage.
Interaction studies in humans have shown no effect on digoxin blood levels.
Interaction studies in humans have shown Bumex to have no effect on warfarin metabolism or on plasma prothrombin activity.
Pregnancy: Bumex should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.
Bumetanide may be excreted in breast milk.
Pediatric Use: Safety and effectiveness below age 18 not established.
ADVERSE REACTIONS. Muscle cramps, dizziness, hypotension, headache and nausea, and encephalopathy (in patients with preexisting liver disease).
Less frequent clinical adverse reactions are weakness, impaired hearing, rash, pruritus, hives, electrocardiogram changes, abdominal pain, arthritic pain, musculoskeletal pain and vomiting.
Other clinical adverse reactions are vertigo, chest pain, ear discomfort, fatigue, dehydration, sweating, hyperventilation, dry mouth, upset stomach, renal failure, asterixis, itching, nipple tenderness, diarrhea, premature ejaculation and difficulty maintaining an erection.
Laboratory abnormalities reported are hyperuricemia, azotemia, hyperglycemia, increased serum creatinine, hypochloremia, hypokalemia, hyponatremia, and variations in CO_2 content, bicarbonate, phosphorus and calcium. Although manifestations of the pharmacologic action of Bumex, these conditions may became more pronounced by intensive therapy.
Diuresis induced by Bumex may also rarely be accompanied by changes in LDH, total serum bilirubin, serum proteins, SGOT, SGPT, alkaline phosphatase, cholesterol, creatinine clearance, deviations in hemoglobin, prothrombin time, hematocrit, platelet counts and differential counts. Increases in urinary glucose and urinary protein have also been seen.
DOSAGE AND ADMINISTRATION:
Oral Administration: The usual total daily dosage is 0.5 to 2.0 mg and in most patients is given as a single dose.
Parenteral Administration: Administer to patients (IV or IM) with GI absorption problem or who cannot take oral. The usual initial dose is 0.5 to 1 mg given over 1 to 2 minutes. If insufficient response, a second or third dose may be given at 2 to 3 hour intervals up to a maximum of 10 mg a day.
HOW SUPPLIED: *Tablets*, 0.5 mg (light green), 1 mg (yellow) and 2 mg (peach), bottles of 100 and 500, Prescription Paks of 30, Tel-E-Dose® cartons of 100. Imprint on tablets: 0.5 mg—ROCHE BUMEX 0.5, 1 mg—ROCHE BUMEX 1; 2 mg— ROCHE BUMEX 2.
Ampuls, 2 ml, 0.25 mg/ml, boxes of ten.
Vials, 2 ml, 4 ml and 10 ml, 0.25 mg/ml, boxes of ten.

P.I. 0985

Roche Laboratories
a division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

5923 037

FRANCIS A COUNTWAY LIBRARY OF MED
EXCHANGE OFFICE
10 SHATTUCK STREET
BOSTON MA 02115

In acute and chronic edema due to CHF

A DIURETIC THAT GIVES YOU PREDICTABLE CONTROL

Bumex®

bumetanide/Roche

0.5-mg, 1-mg and 2-mg scored tablets; 2-ml ampuls and 2-ml, 4-ml and 10-ml vials (0.25 mg/ml)

Please see adjacent page for references and summary of product information.

Copyright © 1987 by Hoffmann-La Roche Inc. All rights reserved.